A Dissertation on

A STUDY ON CLINICOPATHOLOGICAL SPECTRUM OF CUTANEOUS LUPUS ERYTHEMATOSUS AND ITS CORRELATION WITH ANCILLARY TESTS

COIMBATORE MEDICAL COLLEGE

COIMBATORE

Dissertation Submitted

with partial fulfilment of the regulations

for the award of the degree of

M.D. DEGREE IN

PATHOLOGY (BRANCH III)

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY

CHENNAI - 600 032

MAY 2019

DECLARATION

I, hereby declare that the dissertation entitled **"A STUDY ON CLINICOPATHOLOGICAL SPECTRUM OF CUTANEOUS LUPUS ERYTHEMATOSUS AND ITS CORRELATION WITH ANCILLARY TESTS''** is a bonafide research work done by me in the Department of Pathology, Coimbatore Medical College during the period from January 2017 to June 2018 under the guidance and supervision of Dr. **A. DHANALAKSHMI, M.D,** Associate Professor, Department of Pathology, Coimbatore Medical College.

This dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University, Chennai towards the partial fulfilment of the requirement for the award of M.D., Degree (Branch III) in Pathology. I have not submitted this dissertation on any previous occasion to any University for the award of any Degree.

Place : Coimbatore **DR. K.BRINDHA**

Date :

CERTIFICATE

This is to certify that dissertation entitled " **A STUDY ON CLINICOPATHOLOGICAL SPECTRUM OF CUTANEOUS LUPUS ERYTHEMATOSUS AND ITS CORRELATION WITH ANCILLARY TESTS''** is a record of bonafide work done by **Dr.K.BRINDHA**, a postgraduate student in the Department of Pathology, Coimbatore Medical College, Coimbatore under the guidance and supervision of **Dr. A. DHANALAKSHMI, M.D.,** Associate Professor, Department of Pathology, Coimbatore Medical College, Coimbatore and submitted in partial fulfilment of the regulation of the Tamilnadu Dr. M.G.R. Medical University, Chennai towards the award of M.D., Degree (Branch III) in Pathology.

Guide
DR. A. DHANALAKSHMI, M.D.,
Associate professor,
Department of Pathology,
Coimbatore Medical College,
Coimbatore.

Head of the department
DR. C. LALITHA, M.D.,
Professor & Head
Department of Pathology,
Coimbatore Medical College,
Coimbatore.

Dr. B. ASOKAN, M.S., MCh.,
Dean,
Coimbatore Medical College,
Coimbatore.

Coimbatore Medical College

COIMBATORE, TAMILNADU, INDIA - 641 014

(Affiliated to The Tamilnadu Dr. MGR Medical University, Chennai)

ETHICS COMMITTEE

CERTIFICATE

Name of the Candidate:		**Dr.K.Brindha**
Course	:	**MD (Pathology) Post Graduate**
Period of Study	:	**1 year**
College	:	**Coimbatore Medical College & Hospital.**
Dissertation Topic	:	**A study on clinicopathological spectrum of cutaneous lupus erythematosus and its correlation with ancillary tests.**

The Ethics Committee, Coimbatore Medical College has decided to inform that your Dissertation Proposal is accepted and you are permitted to proceed with the above Study.

21.12.16

Member Secretary
Ethics Committee

URKUND

Urkund Analysis Result

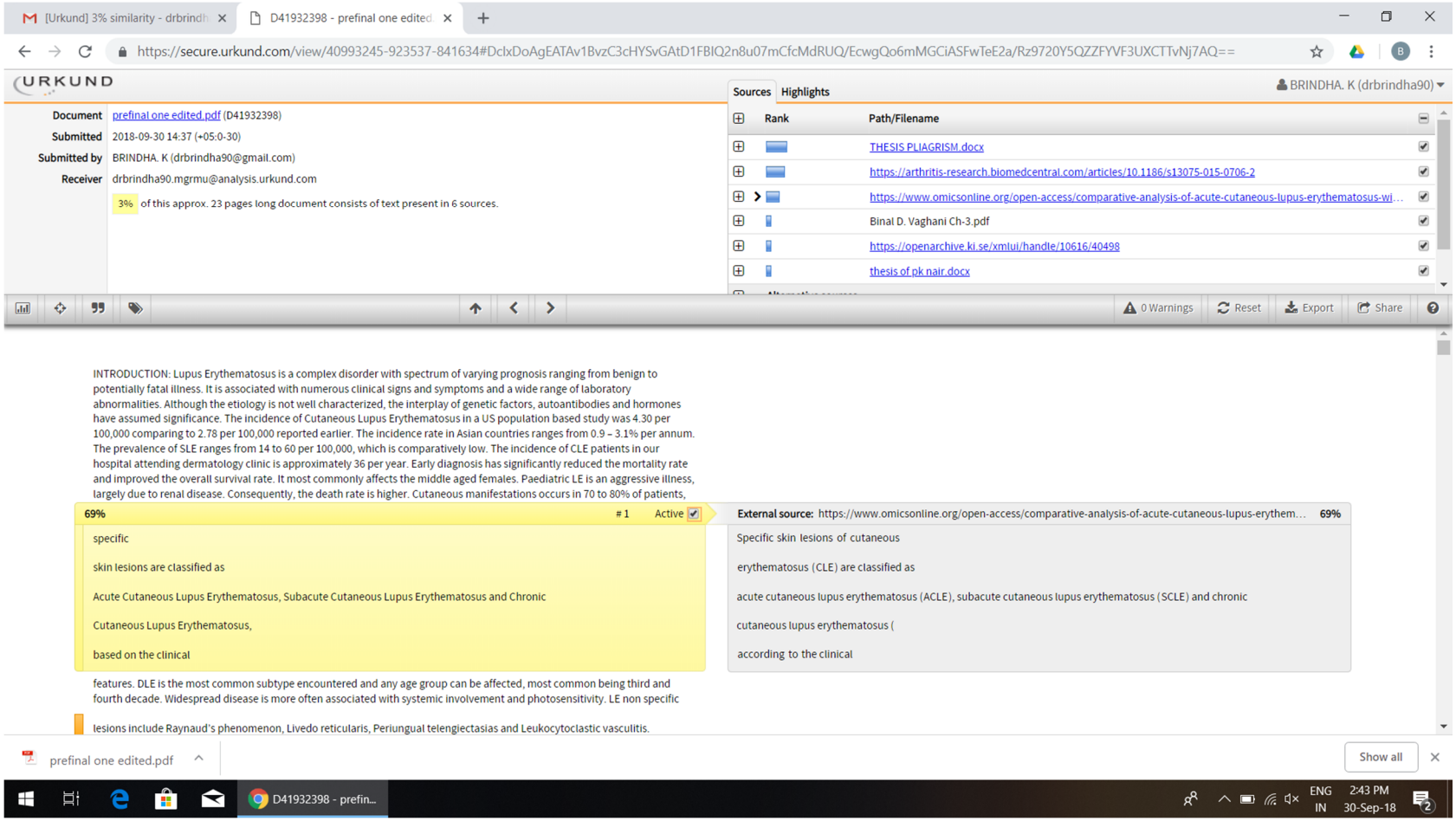
Analysed Document:	prefinal one edited.pdf (D41932398)
Submitted:	9/30/2018 11:07:00 AM
Submitted By:	drbrindha90@gmail.com
Significance:	3 %

Sources included in the report:

THESIS PLIAGRISM.docx (D31066560)
Binal D. Vaghani Ch-3.pdf (D19892148)
thesis of pk nair.docx (D31155161)
https://openarchive.ki.se/xmlui/handle/10616/40498
https://arthritis-research.biomedcentral.com/articles/10.1186/s13075-015-0706-2
https://www.omicsonline.org/open-access/comparative-analysis-of-acute-cutaneous-lupus-erythematosus-withsubacute-and-chronic-cutaneous-lupus-erythematosus-clinical-andimm-2167-7921-1000185.php?aid=66720

Instances where selected sources appear:

14


[Urkund] 3% similarity - drbrindh
D41932398 - prefinal one edited
https://secure.urkund.com/view/40993245-923537-841634#DclxDoAgEATAv1BvzC3cHYSvGAtD1FBIQ2n8u07mCfcMdRUQ/EcwgQo6mMGCiASFwTeE2a/Rz9720Y5QZZFYVF3UXCTTvNj7AQ==
URKUND
BRINDHA. K (drbrindha90)
Document prefinal one edited.pdf (D41932398)
Submitted 2018-09-30 14:37 (+05:0-30)
Submitted by BRINDHA. K (drbrindha90@gmail.com)
Receiver drbrindha90.mgrmu@analysis.urkund.com
3% of this approx. 23 pages long document consists of text present in 6 sources.
Sources
Highlights
Rank
Path/Filename
THESIS PLIAGRISM.docx
https://arthritis-research.biomedcentral.com/articles/10.1186/s13075-015-0706-2
https://www.omicsonline.org/open-access/comparative-analysis-of-acute-cutaneous-lupus-erythematosus-wi...
Binal D. Vaghani Ch-3.pdf
https://openarchive.ki.se/xmlui/handle/10616/40498
thesis of pk nair.docx
0 Warnings
Reset
Export
Share
INTRODUCTION: Lupus Erythematosus is a complex disorder with spectrum of varying prognosis ranging from benign to potentially fatal illness. It is associated with numerous clinical signs and symptoms and a wide range of laboratory abnormalities. Although the etiology is not well characterized, the interplay of genetic factors, autoantibodies and hormones have assumed significance. The incidence of Cutaneous Lupus Erythematosus in a US population based study was 4.30 per 100,000 comparing to 2.78 per 100,000 reported earlier. The incidence rate in Asian countries ranges from 0.9 – 3.1% per annum. The prevalence of SLE ranges from 14 to 60 per 100,000, which is comparatively low. The incidence of CLE patients in our hospital attending dermatology clinic is approximately 36 per year. Early diagnosis has significantly reduced the mortality rate and improved the overall survival rate. It most commonly affects the middle aged females. Paediatric LE is an aggressive illness, largely due to renal disease. Consequently, the death rate is higher. Cutaneous manifestations occurs in 70 to 80% of patients,
69%
1
Active
specific
skin lesions are classified as
Acute Cutaneous Lupus Erythematosus, Subacute Cutaneous Lupus Erythematosus and Chronic
Cutaneous Lupus Erythematosus,
based on the clinical
External source: https://www.omicsonline.org/open-access/comparative-analysis-of-acute-cutaneous-lupus-erythem...
69%
Specific skin lesions of cutaneous
erythematosus (CLE) are classified as
acute cutaneous lupus erythematosus (ACLE), subacute cutaneous lupus erythematosus (SCLE) and chronic
cutaneous lupus erythematosus (
according to the clinical
features. DLE is the most common subtype encountered and any age group can be affected, most common being third and fourth decade. Widespread disease is more often associated with systemic involvement and photosensitivity. LE non specific
lesions include Raynaud's phenomenon, Livedo reticularis, Periungual telengiectasias and Leukocytoclastic vasculitis.
prefinal one edited.pdf
Show all
D41932398 - prefin...
ENG
IN
2:43 PM
30-Sep-18

CERTIFICATE –II

This is to certify that this dissertation work titled **"A STUDY ON CLINICOPATHOLOGICAL SPECTRUM OF CUTANEOUS LUPUS ERYTHEMATOSUS AND ITS CORRELATION WITH ANCILLARY TESTS"** of the candidate **DR. K. BRINDHA** with registration number 201613253 for the award of MD Degree in the branch of PATHOLOGY. I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **3 percentage** of plagiarism in the dissertation.

Guide & Supervisor sign with Seal

ACKNOWLEDGEMENT

To begin with, I thank the almighty for bestowing his blessings on me for completing this dissertation successfully.

I wish to thank our beloved Dean, **Dr. B. ASOKAN, M.S., MCh.,** Coimbatore Medical College and Hospital, Coimbatore for permitting me to conduct this study.

I express my heartfelt thanks to our Head of the Department, Professor **Dr.C.LALITHA, M.D.,** Department of Pathology, Coimbatore Medical College, Coimbatore for her immense guidance and support in conducting this study.

I express my gratitude and sincere thanks to my guide **DR. A. DHANALAKSHMI, M.D.,** Associate Professor, Department of Pathology, Coimbatore Medical College, Coimbatore. This dissertation bears her valuable suggestions, constant encouragement and support without which I would not have been able to finish this dissertation successfully.

I owe my gratitude to all my associate professors , assistant professors and all my teachers of Department of Pathology, Coimbatore Medical College, for their timely advice and valuable suggestions through the course of my work.

I thank the Department of Dermatology, Coimbatore Medical College, Coimbatore, for providing clinical cases, valuable support and guidance to make this dissertation possible and successful one.

I thank all the lab technicians working in Department of Pathology, Coimbatore Medical College, Coimbatore for their sincere and timely technical support.

I thank my DAD **Mr. K. Kanagaraj**, whom I miss so much, for always having faith in me in whatever I do and constant encouragement and now for bestowing his blessings on me in making this dissertation , a successful one.

I thank my mom **Mrs. K. Sakunthala**, my sister, my brother, my niece and other family members who stood by me as pillars of strength all the way through this endeavour.

I thank my friends, juniors and seniors for their constant support and encouragement throughout this study.

DR. K. BRINDHA

TABLE OF CONTENTS

SL.NO	TITLES	PAGE.NO
1	INTRODUCTION	1
2	AIMS AND OBJECTIVES	3
3	REVIEW OF LITERATURE	4
4	MATERIALS AND METHODS	54
5	OBSERVATION AND RESULTS	62
6	DISCUSSION	74
7	SUMMARY	82
8	CONCLUSION	85
9	BIBLIOGRAPHY	86
10	ANNEXURES	
	PROFORMA	98
	CONSENT FORM	100
	MASTER CHART	101

LIST OF TABLES

S.NO	NAME OF TABLES	PAGE NO
1.	Lupus band test of lesional and non lesional sites in various subtypes of CLE	43
2.	Differential diagnosis of CLE	50
3.	Mean age of the study	62
4.	Age distribution of CLE	63
5.	Gender distribution of CLE	64
6.	Gender distribution among different age groups in the study	65
7.	Clinical features of CLE	66
8.	Site involvement in CLE	67
9.	Pathological diagnosis in the study	68
10.	Pathological diagnosis among different age groups in the study	69
11.	Pathological diagnosis with duration of symptoms in the study	70
12.	Histopathological features of various subtypes of CLE	71
13.	Special stain application (PAS with Alcian blue)	73
14.	Comparison of histopathological features of ACLE with Karumbaiah et al study	77

S.NO	NAME OF TABLES	PAGE NO
15.	Comparison of histopathological features of SCLE with various studies	78
16.	Comparison of histopathological features of DLE with various studies	79
	FLOW CHART	
1.	Pathogenesis of SLE.	33

LIST OF CHARTS

S.NO	NAME OF CHARTS	PAGE NO
1.	Age distribution of CLE	63
2.	Gender distribution of CLE	64
3.	Gender distribution among different age groups in the study	65
4.	Clinical features of CLE	66
5.	Site involvement in CLE	67
6.	Pathological diagnosis in the study	68
7.	Pathological diagnosis among different age groups in the study	69
8.	Pathological diagnosis with duration of symptoms in the study	70
9.	Histopathological features of various subtypes of CLE	72
10.	Special stain application (PAS with Alcian blue)	73

LIST OF FIGURES

SL.NO	NAME OF FIGURES
1.	Classification of CLE and its variants
2.	Maculopapular eruptions and malar rash in ACLE
3.	IIF of Hep 2 cell lines
4.	DIF in DLE- Deposits of IgM and IgG
5.	DIF in SLE – Deposits of IgG and IgA
6.	H & E section – Epidermal atrophy and follicular plugging – Low power (100X)
7.	H & E section – Follicular plugging , periadnexal and perivascular inflammation – Low power (100X)
8.	H & E section – Periadnexal and perivascular inflammation – Scanner view (40X)
9.	H & E section – Follicular plugging and periadnexal inflammation –Low power (100X)
10.	H & E section – Perivascular and periadnexal inflammation – High power (400X)
11.	H & E section – Basal cell vacuolar degeneration - High power (400X)
12.	H & E section – Hyperkeratosis and basement membrane thickening – High power (400X)

SL.NO	NAME OF FIGURES
13.	PAS with Alcian blue stain – Basement membrane thickening – High power (400X)
14.	PAS with Alcian blue stain – Hyperkeratosis, focal basement membrane thickening and basal cell degeneration – High power (400X)
15.	PAS with Alcian blue stain – Basal cell vacuolar degeneration and mild basement membrane thickening – High power (400X)
16.	PAS with Alcian blue stain – Interstitial dermal mucin – Low power (100X)
17.	PAS with Alcian blue stain – Interstitial dermal mucin – High power (400X)
18.	H & E section – Vasculitis – High power (400X)

LIST OF ABBREVIATIONS

CLE	–	Cutaneous Lupus Erythematosus
ACLE	–	Acute Lupus Erythematosus
SLE	–	Systemic Lupus Erythematosus
SCLE	–	Subacute Lupus Erythematosus
DLE	–	Discoid Lupus Erythematosus
DIF	–	Direct ImmunoFluorescence
IIF	-	Indirect ImmunoFluorescence
Ig	–	Immunoglobulin
UV	–	Ultraviolet
IL	–	Interleukin
TNF	–	Tumour Necrosis Factor
ROS	–	Reactive Oxygen Species
PLE	–	Polymorphic Light Eruption
SCC	–	Squamous Cell Carcinoma
LP	–	Lichen Planus
PAS	–	Periodic Acid Schiff
ANA	–	Anti Nuclear Antibody
IHC	–	Immunohistochemistry
ARA	–	American Rheumatism Association
DEJ	–	Dermo Epidermal Junction
PAV	–	Poikiloderma Atrophicans Vasculare

INTRODUCTION

Lupus Erythematosus is a complex disorder with spectrum of varying prognosis ranging from benign to potentially fatal illness. It is associated with numerous clinical signs and symptoms and a wide range of laboratory abnormalities. Although the etiology is not well characterized, the interplay of genetic factors, autoantibodies and hormones have assumed significance.

The incidence of Cutaneous Lupus Erythematosus in a US population based study was 4.30 per 100,000 comparing to 2.78 per 100,000 reported earlier. The incidence rate in Asian countries ranges from 0.9 – 3.1% per annum. The prevalence of SLE ranges from 14 to 60 per 100,000, which is comparatively low. The incidence of CLE patients in our hospital attending dermatology clinic is approximately 36 per year.

Early diagnosis has significantly reduced the mortality rate and improved the overall survival rate. It most commonly affects the middle aged females. Paediatric LE is an aggressive illness, largely due to renal disease. Consequently, the death rate is higher.

Cutaneous manifestations occurs in 70 to 80% of patients, of which specific skin lesions are classified as Acute Cutaneous Lupus Erythematosus, Subacute Cutaneous Lupus Erythematosus and Chronic

Cutaneous Lupus Erythematosus, based on the clinical features. DLE is the most common subtype encountered and any age group can be affected, most common being third and fourth decade. Widespread disease is more often associated with systemic involvement and photosensitivity. Non-specific lesions of Lupus Erythematosus include Raynaud's phenomenon, Livedo reticularis, Periungual telengiectasias and Leukocytoclastic vasculitis. These features are more often observed in SLE. Antinuclear antibody is present in 90 - 95% of SLE, 30 - 35% of DLE and 50% with generalized DLE. 10% of normal population can have ANA at low concentration. LE should be distinguished from the other dermatosis with overlapping histopathological features like Lichen Planus and Poikiloderma.

The aim of this study is to analyze the clinical and histopathological features of CLE and to identify the most common and minimum histopathological features in various subtypes of CLE for early diagnosis in patients attending Department of Dermatology, at CMCH.

AIM OF THE STUDY

To study and analyze the spectrum of Cutaneous Lupus Erythematosus and correlate the clinicopathological features with application of special stains over a period of one and a half years at CMCH.

OBJECTIVES

1. To study the epidemiology and clinicopathological spectrum of Cutaneous Lupus Erythematosus at CMCH in one and a half years period.

2. To identify the most common histopathological features in various types of Cutaneous Lupus Erythematosus.

3. To analyze the utility of special stains in different subtypes of CLE.

REVIEW OF LITERATURE

Lupus erythematosus is an autoimmune, chronic inflammatory disorder of connective tissue, which commonly affects middle aged women. It is of unknown etiology. The clinical manifestation of LE ranges from localized cutaneous eruption to total systemic illness. Cutaneous form is more common than SLE.

In 23 to 28% of systemic lupus cases, cutaneous lesions are the presenting symptoms. 72 to 82% of SLE patients present with atleast one cutaneous symptom through their course of illness [(1)].

Cutaneous LE is subdivided depending on the morphology of lesion and its duration into acute, subacute or chronic. The differentiaton of subtype is based on comparison of clinical, histological and immunofluorescence findings. Histopathological examination along with Immunofluorescence and serological studies are very important for the evaluation of lupus erythematosus.

THREE MAJOR CLINICAL VARIANTS :

1. Chronic LE - includes DLE, Lupus panniculitis, Chilblain lupus and Tumid lupus - have only skin predominant disease.

2. Subacute LE - Cutaneous lesion with mild systemic illness

3. Acute LE – Multisystem disease

SCLE - intermediate form between DLE and SLE[2].

In both conditions, biochemical, hematological and immunohistochemical findings are similar.

Overt SLE may develop in patients with DLE in about 1.3[3] to 6.5%[4,5].

In chronic phase of SLE, typical lesion of DLE can occur [6].

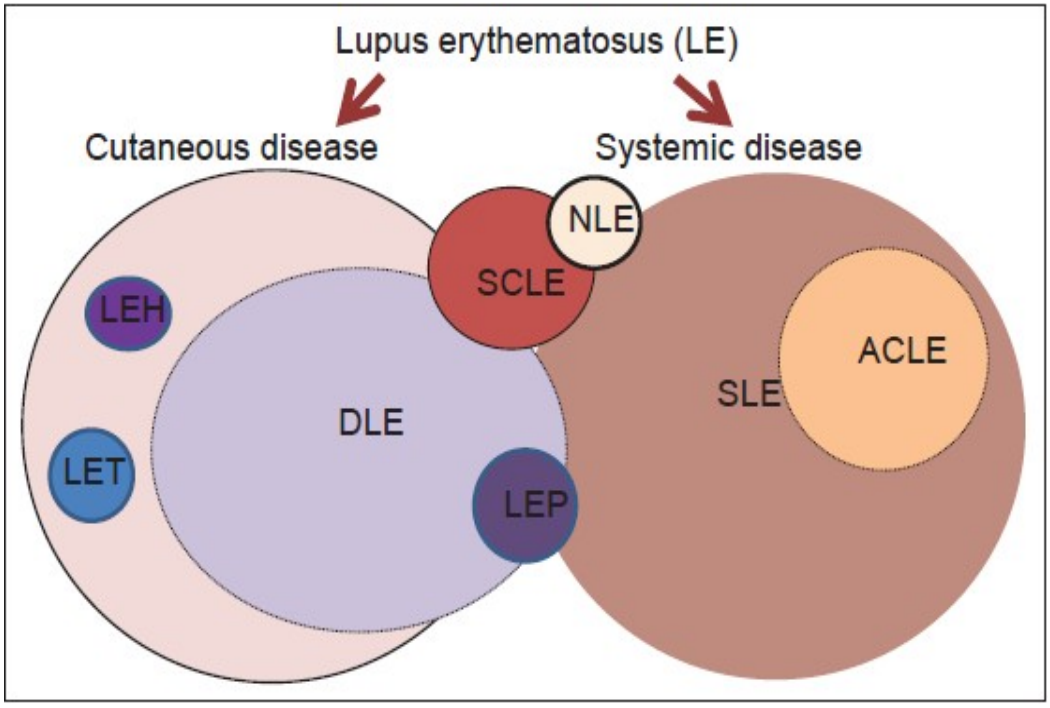


Figure 1 : Classification of Cutaneous Lupus Erythematosus and its variants [7].

Patients with disseminated DLE (22%) have more risk than in DLE limited to head and neck [5]. Uninvolved skin in patients with SLE can have complement and Ig deposit, whereas it is absent in patients with DLE [8].

Incidence of CLE is 4.30 per 1,00,000; age and prevalence of SLE in India ranges from 14 to 60 per 1,00,000[9].

PATHOPHYSIOLOGY OF CUTANEOUS LUPUS ERYTHEMATOSUS: [10]

The pathophysiology of LE includes interactions between the environment, genetics, and immune systems [adaptive and innate] [11].

GENETICS:

MAJOR HISTOCOMPATIBILITY COMPLEX:

The different genetic alterations associated with different type of CLE are as follows:

ACLE - HLA B8, DR3, DQA1 and DRB1

SCLE - HLA DR3 and DR2, positivity for RO SSA autoantibodies

DLE - HLA DQA1 and DRB1

COMPLEMENT DEFICIENCY :

ACLE - Congenital C1q deficiency. Post apoptotic immunogenic material are being cleared by C1q.

SCLE - C1qA single nucleotide polymorphism and lower C1 serum protein levels.

DLE like skin lesions - hereditary deficiencies of C2 and C4.

TNF-alpha:

TNF-alpha (Primary cytokine) plays a vital role in release of cytokines and activation of immune cells, which causes tissue destruction. It also promotes increased expression of auto antigens which lead to autoantibody formation. Polymorphism of TNF alpha promoter is commonly seen in SCLE.

TYK2, IRF5 and CTLA4:

These are associated with CLE.

TYK2, which is involved in DLE, is a janus kinase, which binds to INF-alpha receptor and promotes cytokine signaling.

IRF5- a transcription factor which regulates type I interferon is involved in SCLE and DLE. Increased expression of IRF5 causes production of type I interferon and associated with inflammatory response. It causes UV irradiated skin changes.

CTLA4 regulates T cell response to stimuli. The variants of CTLA4 prevent appropriate limitations of T cell response to inflammation.

ITGAM POLYMORPHISM:

It encodes alpha chain of $alpha_m beta_2$ integrin, which is a cell surface receptor associated with inflammation. It is present in macrophages , dendritic cells and neutrophils. Polymorphism of ITGAM causes abnormal removal of apoptotic cells , impaired phagocytosis, and leucocyte trafficking. It is more often associated with DLE.

TREX1:

Heterozygous missense mutation in TREX1 is associated with familial chilblain lupus. TREX1, encodes the 3'-5'repair exonuclease1, which causes nucleoside mono phosphates excision from 3' termini of DNA. Mutations in TREX1 causes defective apoptosis, abnormal clearance of DNA and induces autoimmunity.

UV RADIATION:

UVB & UVA radiation causes DLE (42%), SCLE (64%) and SLE (25%) [12].

PHOTOSENSITIVITY:

Photosensitivity includes wide range of symptoms in response to light. Anti Ro antibodies appears to relate to photosensitivity. Keratinocytes, in response to or radiation causes accumulation of cytokines and pro inflammatory molecules. It also causes apoptosis, leading to relocalization of auto antigens. These are common in DLE.

UV radiation causes recruitment of immune cells such as T-lymphocytes, myeloid dendritic cells and plasmacytoid dendritic cells along with production of chemokines and cytokines (IL1 <TNF alpha), to induce inflammation by recruiting immune cells[13,14].

APOPTOSIS :

Normally, apoptosis occurs in Stratum granulosum. Suprabasilar keratinocytes are more susceptible to premature apoptosis induced by external agents. The mechanism involved in keratinocyte apoptosis are DNA damage, ROS production and activation of Fas and Fas ligand [15].

Norris et al [16] demonstrated increase number of apoptotic cells in basal layer in DLE , whereas it is seen in suprabasilar epidermis in SCLE

Kuhn et al [17] demonstrated that due to impaired clearance, there is accumulation of apoptotic cells in UV induced DLE lesions.

Chen et al[18] demonstrated that decreased clearance or phagocytosis of apoptotic cells occur due to autoantibodies against macrophage receptors.

AUTO ANTIBODIES:

Various auto antibodies are associated CLE, of which anti Ro/SSA and anti-La/SSB are most important.

Biazar et al [19] demonstrated that anti –Ro/SSA were detected in 72.1% (SCLE), 47.4% (ACLE) and 22% (DLE). ACLE patients who were found with anti Ro/SSA positive, were more photosensitive than patients with negative anti – Ro/SSA. Anti-La/SSB were detected in 36.2% (SCLE), 27.5 (ACLE) and 7.0% (DLE). No difference in photosensitivity were reported in patients with positive / negative anti La/SSB.

Li.et al [20] & Wasicek and Reichlin[21], demonstrated that patients with both anti Ro/SSA and anti La/SSB showed high occurrence of

photosensitivity , discoid rash, hematological involvement and nephritis. Patients with anti RNP, anti SM and anti APL demonstrated high occurrence of malar rash.

Regarding serum immunoglobulin levels, Jost et al[22] demonstrated that immunoglobulins - IgG, IgM and IgA antinuclear antibody, were elevated in SLE than DLE. Ratio of IgG to IgM was increased in SLE than DLE.

CHRONIC LUPUS ERYTHEMATOSUS:

CLINICAL VARIANTS:

It includes

a) Discoid LE – Localized, Disseminated and Hypertrophic LE
b) Tumid LE
c) LE panniculitis
d) Chilblain Lupus

It commonly involves the face including nose and malar areas, ears, oral mucosa, scalp and lips. Middle aged females are usually affected. It consists of well defined, red scaly / infiltrated plaques, which shows follicular plugging and adherent thick scales. These lesions heal with scarring, atrophy and pigmentation [23].

Squamous cell carcinoma, basal cell carcinoma and atypical fibroxanthoma can occur in patients with LE [24]. SCC is a very rare complication [35]. Conversion of DLE to SLE is rare (5 to 10%) [25]. Discoid cutaneous lesions are also found in 14% of patients with SLE [26].

AETIOLOGY:

GENETIC FACTORS:

Familial predisposition occurs in DLE. There is relationship between DLE & Polymorphic light eruption occuring in twins[27] and with common genetic background. It is associated with HLA B7, B8, CW7, DR2, DR3 and DQw1. SCLE and DLE are associated with HLA*01, B*08, DRB1*0301. DLE is associated with A*03, B*07, DRB1*15 [28].

HLA-B7 is associated with patients of age 15 and 39 of both sexes and HLA B8 with females over 40 years[29]. Somatic mutation is involved in the pathogenesis of DLE. Self-destruction is prevented by normal endogenous defence mechanism through lymphocytes function. Environmental factors like stress, UV exposure, trauma, drugs, infections, cold exposure, seasonal changes, pregnancy and hormone replacement therapy also play a role.

Antibodies against reo virus RNA is found in 42% of DLE patients[30].

CLINICAL FEATURES: [31]

Rash is usually the presenting symptom. In a study of 120 patients at Leeds, Raynaud's phenomenon was found in 14%; chill blains in 22%, poor peripheral circulation in 26%, joint pain in one quarter of patients[32]. Localized DLE affects only head and neck regions; generalized skin manifestations are seen in disseminated DLE.

LOCALIZED DLE :

The most common sites affected are face, nose, ears, scalp, legs and trunk. Discoid/well circumscribed lesion vary in size from few mm to 10-15 cm. Lesions can be bilateral, rarely unilateral or symmetrical. Permanent alopecia of scalp occurs in one third of patients [33].

'Tin Tack' sign [34]- The undersurface of the removed adherent scale shows horny plugs (dilated pilosebaceous canals). It also occurs in localized Pemphigus foliaceous.

The dirty brownish yellow surface is rough due to follicular plugging. Warty lesion with erythematous raised edges occurs when there

is marked hyperkeratosis. It frequently occurs on temples, nose, ears, scalp, palms and soles.

Hyperkeratotic or papulo nodular lesion and annular lesions (i.e) plaques with central flattening can also occur. Annular lesion in acute LE may resemble Erythema multiforme. This is known as Rowell's syndrome [35]. White scarred area along with zone of hyperemia or hyper pigmentation occurs. Localized cribriform scarring also occurs on face. Wide follicular pits occurs in concha or triangular fossa of ear. It occurs in one third of cases[36] of DLE and also in SLE.

Rosaceous LE shows erythematous nodules on cheeks, nose, chin and forehead. No pustules are found as in true rosacea. Biopsy is essential to differentiate between LE and rosacea. Calcification, pigmentation, atrophy and scarring also occurs.

DISSEMINATED DLE:

It is more common in women and in cigarette smokers. Lesions are found on hands, palms , toes, trunk and head[23]. Patients present with purplish plaques or 'LE telangiectoides' (i.e) blotchy, persistent reticulate telangiectasia, seen on face, ears, neck, hands, breast and feet. Punctate atrophic scarring occurs after healing.

CHILDHOOD DLE: [37]

It is rare and no female preponderance is seen. It is associated with less photosensitivity and higher incidence of development of systemic disease. Other features are similar to adults.

CHILBLAIN LUPUS: [38]

It is a rare form (constituting 6% of LE patients), seen in middle aged females. It is characterised by erythematous plaques, involving acral areas which are induced by exposure to cold. It can also involve ears and nose. Chilblain remains even after treatment. The histological and immunohistological characteristics is similar to DLE and negative fluorescent band test occurs in non lesional skin.

Patients are Ro antibody positive [39], may also have cold agglutinins or cryofibrinogenemia.

NAIL CHANGES: [40]

The lesion shows subungual hyperkeratosis and nail plate shows reddish blue discoloration along with longitudinal striae. It responds to chloroquine.

MUCOUS MEMBRANE: [41]

Mucous membranes are involved in 24% of patients. Buccal mucosa and palate shows hyperkeratosis and LP like plaques. Lips show redness, thickening, superficial ulceration and crusting.

EYE LESIONS:

Eyelids have erythematous and scaly lesions, commonly in the outer third of lower eyelids [42].

Conjunctiva is congested and edematous. Corneal involvement is rare.

HISTOPATHOLOGY:

1. Stratum corneum – hyperkeratosis with follicular plugging , inconspicuous parakeratosis.

2. Epidermis – flattening and thinning of stratum malpighii. Individual cell necrosis (apoptosis), squamatization of basal layer, loss of undulating rete ridge pattern and dyskeratosis of basilar keratinocytes.

   Colloid bodies (apoptotic keratinocytes) are 10microns in diameter homogeneous, round to ovoid eosinophilic structures, which are

found in lesion with basilar keratinocytes damage. It is seen in DLE, Lichen planus (civatte bodies), poikiloderma, lichenoid keratoses and fixed drug eruptions. It is usually found in lower epidermis or papillary dermis, which are PAS positive ('+'ve) diastase resistant [23] .

Depending on the clinical characteristics of lesion, the changes in epidermis varies. Flattening and thinning of Stratum malpighii may occur. If it is a verrucous lesion, it comprises of hyperkeratotic, hyperplastic and papillomatous epidermis resembling hypertrophic solar keratosis or superficially invading SCC.[43]

Basement membrane – In chronic lesion, the basement membrane, which is usually inconspicuous and delicate, becomes thickened and tortuous not only at DEJ, but also in follicular dermal junctions. This can be demonstrated by PAS stain (PAS positive diastase resistant). Deposition of immune reaction correlates with its location, on DIF.

PAS positive subepidermal basement membrane zone may occur fragmented or absent in areas of basal cell vacuolar degeneration[44]. There is homogenization, thickening and increased PAS reaction intensity in capillaries .

3. Dermis - Lichenoid reaction (interface dermatitis) associated with liquefactive/ vacuolar degeneration in the basal layer (which means vacuolar space between and beneath the basilar keratinocytes). Inflammation is also seen in periadnexal (hair follicle and sebaeceous glands) region and in an interstitial pattern. There is gradual atrophy and disappearance of pilosebaceous units due to inflammatory cells infiltration. Deposition of mucin in interstitium, vasodilation, edema and erythrocyte extravasation are additional features. Pigmentary incontinence occurs (i.e) because of basal cell hydropic degeneration, melanophages lose their melanin.

4. Subcutaneous tissue – minimal inflammatory infiltrates.

5. Changes in blood vessels:

   Blood vessels are dilated and surrounded by edema. Proliferative and obliterative changes are absent. There is increase in deposition of ground substance (i.e) hyaluronic acid, in middle and lower dermis. It is detected by Alcian blue or colloidal iron stains. In early lesions, fibrinoid deposits in the dermis are noted.

Presence of **atleast 2** of following features is essential for diagnosing Lupus erythematosus [31].

1. Basal cell vacuolar degeneration
2. Edema, hyalinization and fibrinoid changes of the connective tissue, most predominantly just below the epidermis.
3. Periappendageal inflammation, constituting lymphocytes, few plasma cells and histiocytes.

The following features are less important.

- Atrophy of epidermis with hyperkeratosis and follicular plugging along with atrophy of pilosebaceous units.
- Basement membrane thickening of epidermis and small vessels.
- In light exposed areas, there is premature elastotic collagen degeneration.

HISTOLOGY OF DISSEMINATED DLE :

On microscopy, the lesion shows epidermal atrophy and dilatation of cutaneous superficial vessels and infiltration of papillary part of corium.

'LE gyratus repens' : along with features of LE, there is migratory gyrate annular erythema.

VARIANTS OF DLE :

TUMID LE: [35]

Tumid LE is the dermal form of LE without any epithelial/ surface involvement [23]. Patients present with non-scarring plaques, papules and nodules without any atrophy or surface ulceration. It usually occurs on neck, face and upper trunk - sun exposed areas. Unique presentation is eyelid erythema and edema in one eye (unilateral). SLE may be present along with this variant or it may develop subsequently [45]. It also develops in treated HIV patients.

Histology :

On microscopy, it shows lymphocytic infiltrates around the dermal perivascular, interstitial and periappendageal regions. Subepidermal edema along with mucin deposition in the stroma is seen. The involvement of epidermis is rare [35]. There is mild atrophy of epidermis along with focal thickening of basement membrane and sparse lymphocytic infiltrate than in Jessner's lymphocytic infiltration. These features supports the consideration of these 2 disorders in same spectrum [35].

HYPERTROPHIC /VERRUCOUS LE: [23,35]

In about 2% of patients with DLE, there is excessive epithelial proliferation, which present as verrucous lesions. It occurs on arms, face, hands and rarely back. Clinically they may be mistaken for Lichen planus or keratoacanthomas. Diagnostic clue is the presence of typical lesion of DLE elsewhere.

Histology :

Epidermis shows hyperkeratosis, papillomatosis and hyperplastic epithelium. Lower portion of epidermis shows dyskeratotic keratinocytes. Dermoepidermal junction shows band like mononuclear infiltration. It may resemble SCC, mainly in shave biopsy [35]. At the tip of epidermal downgrowth, elastic fibres are preserved, which differentiates it from SCC.

A variant of this type shows acanthosis, elongation of rete ridges along with cup shaped keratin filled crater and scant mononuclear infiltration.

LE HYPERTROPHIC ET PROFUNDUS: [46]

A rare destructive variant of hypertrophic DLE is LE hypertrophicus et profundus. Patients presents with tender scaly lesions,

which progresses to warty growth, later forming a brown to black tar like plaque. It is associated with subcutaneous necrosis, serological abnormalities and antibody to extractable nuclear antigen. On superficial shave biopsy, this may be misdiagnosed as SCC.

LE PROFUNDUS/ PANNICULITIS: [23]

It is an unusual type of LE where subcutaneous tissue is additionally involved. Females of any age can be affected. It can occur in DLE ($2/3^{rd}$ of patients) and SLE. Patients present with multiple, persistent, discrete, firm, rubbery nodules on arms, face (cheeks), chest , buttocks, legs and back. It heals with depressed scars. It commonly involves deep dermis and subcutaneous tissue, forming well defined nodules.

Histology:

On microscopy, lobules of lymphohistiocytic infiltrates along with plasma cells are seen in the subcutaneous tissue. Vascular changes includes prominent endothelium, thrombosis, calcification or perivascular fibrosis showing onion skin appearance. Hyalinization of lobules occurs due to fat necrosis with fibrin deposition. Mucin deposition in stroma is also found. It also includes the changes occurring in LE such as

epidermal atrophy, basal cell vacuolar degeneration and follicular plugging [47].

The characteristic histopathological findings is sufficient to diagnose this variant in the absence of cutaneous and systemic lesions of LE [47].

Differential diagnosis :

Subcutaneous panniculitis like T cell lymphoma has to be differentiated using IHC .

PROGNOSIS: [4]

If the DLE skin lesions are left untreated, they persist. Lesions with little scaling may heal off completely in a month or two. If there is long standing scaling, slowly scarring occurs. Of these patients 57 % present with scarring; 35% with scarring alopecia and 35% can have pigmentary abnormalities [48]. 50% of patients may have complete remission over few years [4]. When exposed to sunlight, cold, trauma or mental stress, relapses occur.

Risk of developing SLE is 6.5% [5]. It is more common in disseminated DLE (22%) than in DLE of head and neck (1.2%). The course of the disease is not altered by immunological or biochemical

abnormalities. Careful monitoring of patients with signs of neuropathy, arthralgia and ANA titres of 1:320 or more should be done.[49]

SUBACUTE CUTANEOUS LUPUS ERYTHEMATOSUS :

DEFINITION: [50]

A Specific subset of lupus with mainly cutaneous disease and mild form of systemic disease, is closely associated with antibodies to Ro/SS-A antigen. It represents about 9% of all LE cases [23]. It has good prognosis.

AETIOLOGY: [50]

Ultraviolet light causes increase in synthesis and expression of Ro/SS-A antigens on the surface of keratinocytes in epidermis, where it binds to antibody and causes the disease [51]. Higher titres of Ro/SS-A are found in SCLE with SLE than patients with only SCLE [52]. The disease activity does not depend on the antibody titres [35]. SCLE is associated with HLA-DR3 and B8 (most common), also HLA-A1, DQ2, DRw2 and C4 null haplotype. Decreased levels of C1q antigen is due to Single Nucleotide Polymorphism [53].

CLINICAL FEATURES : [50,23]

It presents as erythematous, non-scarring papulosquamous ($2/3^{rd}$) or annular to polycyclic lesion ($1/3^{rd}$). It commonly affects adults, on extensor surface of arms, upper trunk, dorsum of hands and fingers. Hyperkeratosis and follicular plugging are rarely found. These lesions heal by forming telangiectasis and hypopigmentation. Other features includes photosensitivity, non-scarring alopecia, Raynaud's phenomenon, Mouth ulceration and Livedo reticularis. It is associated with other disorders such as Morphea, Sjogren's syndrome, Rheumatoid arthritis , Crohn's disease, Lichen planus , Psoriasis, Porphyria cutanea tarda etc. 50% of patients fulfill the criteria of SLE (by ARA).

SCLE occurs during PUVA treatment, IFN-beta1a therapy and radiation therapy. It is also associated with breast carcinoma, hepatocellular carcinoma, meningioma, lung carcinoma, prostrate carcinoma, Hodgkin's disease and Squamous cell carcinoma of head and neck [50].

HISTOPATHOLOGY: [23]

Histologic changes occurs predominantly at dermal epidermal interface. It includes,

1. Hydropic / vacuolar degeneration of basilar keratinocytes, leading to formation of clefts and subepidermal vesicles.
2. Prominent epidermal atrophy
3. Colloid bodies are found in lower epidermis and papillary dermis.
4. Dermis shows extensive edema, fibrinoid deposits and extravasation of erythrocytes. Deposition of mucin in superficial dermis is seen [35].

Hyperkeratosis, follicular plugging, inflammatory infiltrates and basement membrane thickening are less prominent than in DLE.

Atrophy of pilosebaceous units helps to distinguish between DLE and SCLE, which is more prominent in DLE.

NEONATAL LUPUS ERYTHEMATOSUS: [23]

It is a rare disorder. The onset of disease is at birth to 2 months and starts resolving around 6 months with decrease in maternal antibodies. Clinical and histological characteristics are similar to SCLE. It occurs in

neonates, due to passage of maternal IgG ANA (anti Ro / SSA, anti La / SSB or anti U1 RNP auto antibodies) from the mother through the placenta . It commonly involves scalp, periorbital region and extremities.

The most common auto antibodies are anti RO / SSA in about 95% of patients. It is associated with annular to polycyclic, non-scarring lesions, photosensitivity, mild hemolytic anemia, leucopenia, transient thrombocytopenia and congenital heart block (50%). Individuals with neonatal LE may develop SLE around 40 years of age [23].

ACUTE LUPUS ERYTHEMATOSUS / SYSTEMIC LUPUS ERYTHEMATOSUS:

DEFINITION :

It is a multisystem disorder, affecting skin, joints and blood vessels along with immunological abnormalities. It usually occurs in adults, especially in females [54].

The criteria for the classificaion of systemic lupus erythematosus by the American Rheumatism Association (ARA) in 1982, was based on clinical and laboratory data [55]. Revised 1982 criteria, does not include subacute CLE as recognised skin manifestation and also recommends skin biopsy. Biopsy from oral or scalp lesions should be avoided [23].

Initially, ARA criteria was established to differentiate between SLE and the other rheumatic diseases. The 11 criteria, are not meant to be either exclusive or restrictive for diagnosing SLE.

It includes [23]

1. Malar rash
2. Discoid rash
3. Photosensitivity
4. Oral ulcer (painless)
5. Non erosive arthritis (involving 2 or > peripheral joints with swelling, tenderness and effusion.)
6. Serositis (pleuritis / pericarditis)
7. Renal disorder (persistent proteinuria exceeding 0.5 g/day or cellular casts)
8. Neurologic disorders (seizures or psychosis).
9. Hematologic disorders (hemolytic anemia ; leucopenia of < 4,000 cu mm; lymphopenia of < 1,500 /mm3 or thrombocytopenia < 1,00,000/mm3).
10. Immunologic disorder (positive lupus erythematosus cell Preparation ; anti DNA in abnormal titre ; antibody to Sm nuclear Antigen ; or false positive serologic test for syphilis).

11. Antinuclear antibody

SLE is diagnosed when **4 or >** of the above features are present simultaneously or serially .

SYSTEMIC LESIONS :

Systemic lesions occur due to deposition of antigen and antibody complexes in organ systems. It is found in skin, blood vessels, kidney and choroid plexus of brain.

- Arthritis occurs commonly
- Most common cause of death in SLE patients is renal disease.
- Serositis – occurs in epicardium, pleura and peritoneum, which shows mononuclear inflammatory cell infiltration and fibrinoid deposits in the vessel wall.
- Spleen – Periarterial fibrosis occurs (i.e) sclerotic collagen fibres are arranged in thick, concentric layer around the vessels.
- Heart - Libman sacks endocarditis also known as verrucous endocarditis, which forms vegetations along the valve leaflets. Mitral and tricuspid valves are commonly affected.
- Antiphospholipid antibody syndrome – 10% of SLE patients have lupus anticoagulants. Thrombosis (Deep vein, pulmonary, renal

and dermal vessels thrombosis), recurrent fetal abortions and thrombocytopenia are common manifestations.

- Anti cardiolipin antibody – more common than lupus anticoagulant. It is associated with thrombosis, essential hypertension and abnormalities of valves, disseminated intravascular coagulation, livedo reticularis and ulcers.

SLE is associated with Rheumatoid arthritis, Polymyalgia, Systemic sclerosis, Sjogren's syndrome, Myasthenia gravis, Hashimoto's thyroiditis, Pernicious anemia, Leukemia, Lymphoma, Von willebrand's disease, Monoclonal gammapathy and Multiple myeloma, Ulcerative colitis, Pemphigus, Pemphigoid, Dermatitis herpetiformis etc [56].

AETIOLOGY :

Etiology of SLE is usually unknown.

GENETIC FACTORS :

Genetic factors plays vital role in pathogenesis of SLE. It has been reported in identical twins [57] and 4% are familial. There is increased incidence of hyperglobulinemia, anti-nuclear antibodies, anti cardiolipin antibodies and impaired suppressor T lymphocyte function. Familial

cases of SLE are commonly associated with C5 -9 complement factor deficiency [58].

AUTOANTIBODIES: [59]

Humoral autoantibodies including disease specific (anti-double stranded DNA and anti-smith antibody) and the commonly found (anti-nuclear and anti Ro antibody) which are the hallmark of SLE. When the homeostatic immunological mechanisms are lost, there is development of these antibodies against tissue antigens, which causes the disease.

Anti DNA antibodies bind to DNA receptor on WBCs, and causes release of IFN gamma from mononuclear cells leading to inflammatory and immunological reactions [60].

Lupus anticoagulant are associated with abortion and thrombosis in SLE patients. Antiribosomal P proteins are associated with lupus psychosis.

OTHER IMMUNE FACTORS:

Patients with SLE are associated with defective cell mediated immunity. In active disease, there is reduction in T cell counts and increase in null cells [61]. Activation of complement pathway occurs, in

which C3a and C5a (anaphylatoxins) are increased during exacerbation of disease. It plays vital role in pathogenesis of vascular lesions.

UV RADIATION:

The role of UV radiation in pathogenesis of SLE is not known, but it tends to precipitate the onset or exacerbate the course of disease [62].

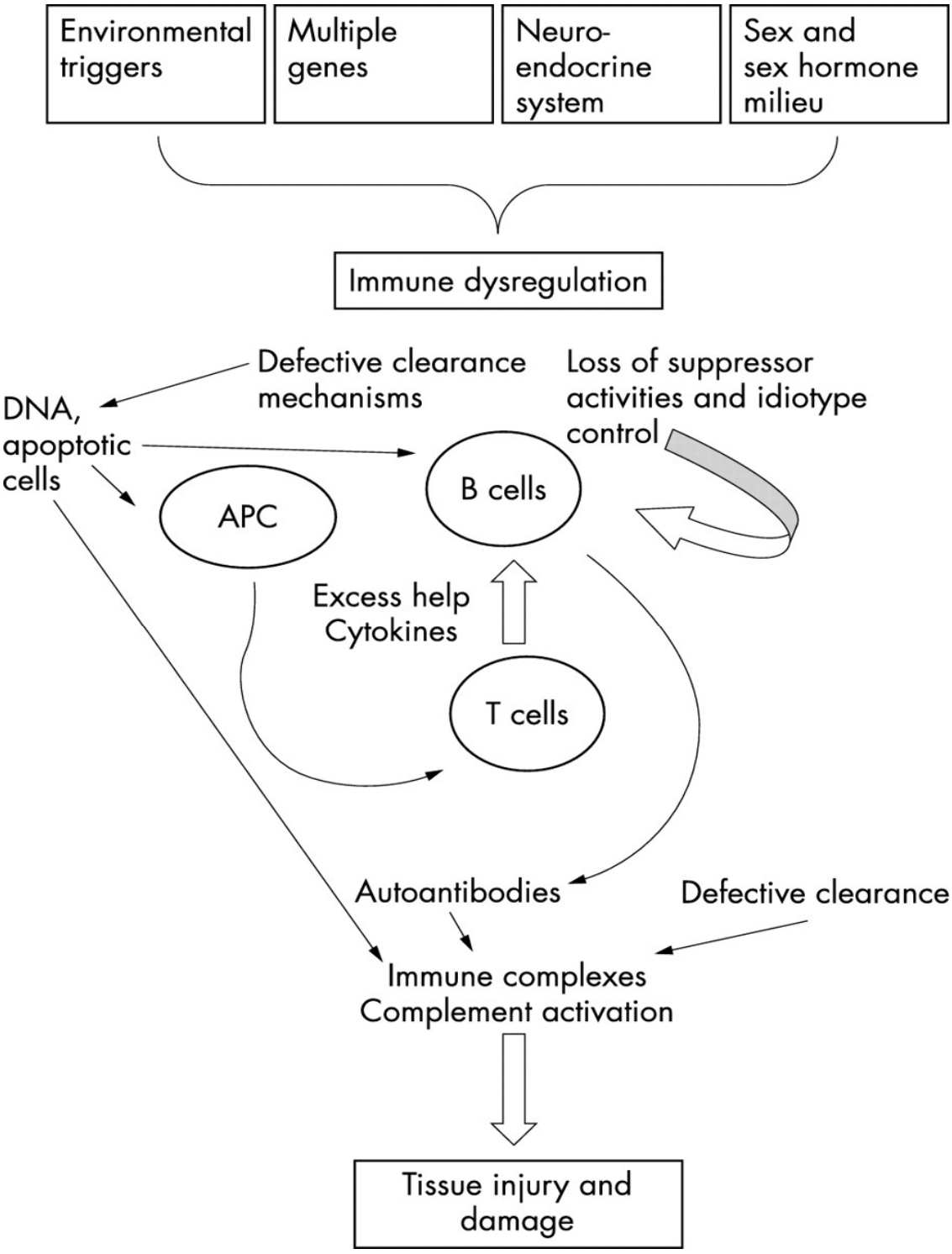
ENVIRONMENTAL FACTORS AND VIRUSES:

Infections, hormones and stress play some role in precipitating the onset of disease. SLE may be associated with increased titres of antibodies to reo virus, rubella and measles.

DRUG INDUCED SLE: [50]

The precipitation of SLE by drugs is well known. There are certain features which distinguishes drug induces LE from spontaneous disease. It commonly occurs in old age and antibodies to histones are common. Renal and CNS involvement and anti DNA antibodies are rare.

Cutaneous involvement may occur as vasculitis, bullous or erythema multiforme like. Drugs which commonly causes drug induced LE or LE like syndromes are antihypertensives (hydralazine), minocycline, anticonvulsants, TNF alpha inhibitors, etc. Patients on drugs should be monitored with ANA and Liver function test regularly.



Flow chart 1: Pathogenesis of SLE [63].

SPECIFIC SKIN LESIONS:

It presents as erythematous, maculopapular eruptions with fine scaling. It commonly involves face (malar area) and elsewhere. Superimposed epidermal necrosis and edema can occur.

Figure 2 : Maculopapular eruptions and malar rash in acute lupus erythematosus patients.

HISTOPATHOLOGY: [23]

Early lesions - erythematous and edematous type show only non-specific changes. Well-developed lesions show features similar to SCLE.

1. Hyperkeratosis without parakeratosis, follicular plugging
2. Hydropic or vacuolar degeneration of basilar keratinocytes

3. Dermis:

It shows edema, extravasation of erythrocytes and fibrinoid deposits. Fibrinoid deposits are fibrin precipitation in ground substance. These are granular, strongly eosinophilic, PAS positive ('+'), diastase resistant deposits between the bundles of collagen, in papillary dermis, in vessels walls and basement membrane zone (main constituents are type IV and VII collagen).

4. Subcutaneous fat :

It is involved in SLE. It is associated with prominent lymphocytic infiltrates and mucin deposition at focal areas. Edema and fibrinoid deposits are found in between the adipocytes. In some cases, leukocytoclastic vasculitis occurs, along with fibrin deposition. Swelling of endothelial cells, inflammatory infiltrates predominantly neutrophils, nuclear dust and stromal haemorrhage are seen.

Hematoxylin bodies in tissues, which represent degenerated nuclear material, are equivalent to LE cells in blood. They are commonly found in visceral lesions than skin lesions [35].

NON SPECIFIC SKIN LESIONS: The following features are not characteristic of CLE, but are frequently observed in SLE.

It includes

1. Raynaud's phenomenon
2. Livedo reticularis
3. Periungual telengiectasias
4. Leukocytoclastic vasculitis.

VARIANTS OF SLE :

FOLLICULAR LUPUS ERYTHEMATOSUS: [35]

In this form of disease, interface dermatitis is confined to the follicles of infundibulum. Perivascular inflammation is seen which distinguishes it from Lichen planopilaris.

BULLOUS SYSTEMIC LUPUS ERYTHEMATOSUS: [64]

It is common in women. Vesicles and bullae may develop. It occurs due to severe basal cell vacuolar degeneration and dermal edema. It usually involves face, neck and upper trunk and are symmetrical. One third of patients have oral lesions. It is commonly associated with glomerulonephritis, anti DNA antibodies and hypocomplementemia.

HISTOPATHOLOGY :

It involves three patterns.

1. Vacuolation of basal layers with formation of subsequent blister. Pustule with subepidermal blister and vasculitis.
2. The neutrophilic pattern with papillary microabscess resembles dermatitis herpetiformis or linear IgA bullous disease. Nuclear dust formation is found in the papillary microabscess, upper dermis and walls of blood vessels.
3. Mononuclear pattern shows subepidermal blister, hyperkeratosis, loss of rete ridges, perivascular and periadnexal inflammatory infiltrates.

Long standing cases produces subepidermal blister with mononuclear inflammatory infiltrates. It occurs due to inflammation and deposition of immune complex, which alters the epidermal dermal interface.

PROGNOSIS :

The course of SLE varies. Acute fulminating cases are less common than subacute cases. Frequency of exacerbations and involvement of organ determines the survival of patient [(2)]. There is high

risk of atherosclerosis, neuropsychiatric disturbances and avascular necrosis with prolonged course of disease[5].

Early diagnosis, avoidance of stress and control of infections by treatment leads to better prognosis. Patients with hemolytic anemia, anti-phospholipid syndrome, thrombocytopenia and CNS involvement have poor prognosis than patients with arthritis. There is no increased risk of malignancy.

INVESTIGATIONS:

INDIRECT IMMUNOFLUORESCENCE TESTS :

Systemic lupus erythematosus, being an autoimmune disorder has autoantibodies directed against intracellular antigens of the cell nucleus. The antigens include double and single stranded DNA (ds DNA and ss DNA), extractable nuclear antigen (ENA) and histones. These are not specific for SLE. Immunodiffusion (ID), Indirect Immunofluorescence (IIF) and Enzyme linked immunosorbent assay (ELISA) are used to detect the antibodies. The type of assay will crucially influence the interpretation of results.

This test shows nuclear, rim, homogenous, speckled and nucleolar patterns. Specific marker is rim pattern and ANA titre of 1:160 or greater. It detects the presence of anti-double stranded DNA antibodies. Lupus

nephritis is associated with presence of anti- Sm antibody. Anti-single stranded DNA is nonspecific and found in many other diseases.

When ANA is negative, presence of anti- Ro/SSA and anti – La/SSB antibodies should be examined, as it is specific for subacute and neonatal LE and SLE with genetic deficiency of complements.

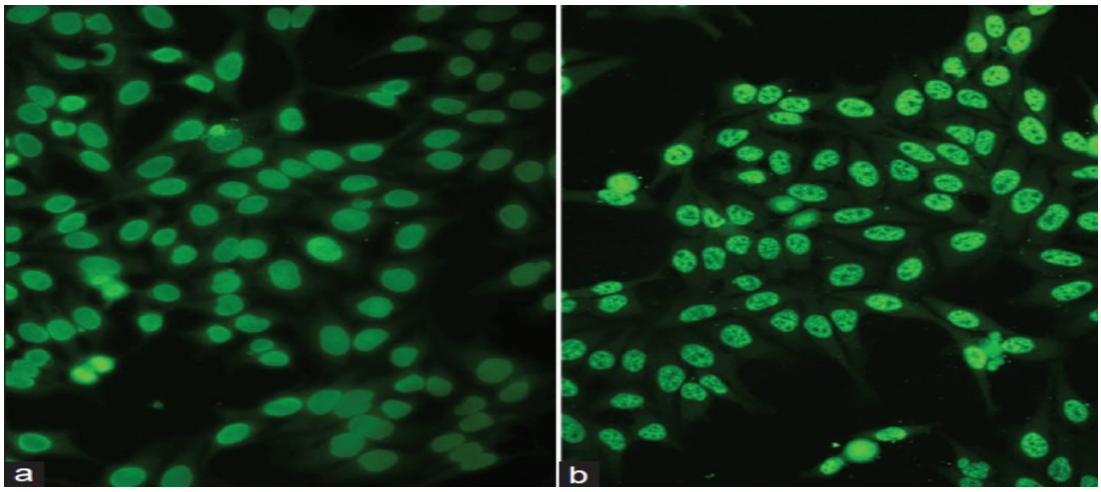


Figure 3: IIF of Hep 2 cell lines a) diffuse homogenous b) speckled pattern of nuclear fluorescence, x 400 [71].

DIRECT IMMUNOFLUORESCENCE TEST :

A 3-4mm skin biopsy sent in saline impregnated gauze or phosphate buffered Saline is sectioned and incubated with fluorescein conjugated antisera to IgG, IgM, IgA and C3. Granular deposition of two or more immune complexes along the dermoepidermal junction is considered positive. The test results vary according to the site of biopsy, duration of lesion and treatment. The involved skin shows positivity in

almost 100% of cases and uninvolved skin from sun exposed areas shows positivity in 90% of cases. Uninvolved skin from sun protected areas show positivity only in 1/3rd of cases.

It may be negative in early stage of disease, treated lesions, during remissions and some drug induced cases.

DLE: [66]

There is homogeneous granular or thread pattern of immunoglobulins – IgA, IgM and complement (IgG and fibrin may be positive) at DEJ in lesional skin for 6 or > weeks in about 80% of patients. It occurs due to passive absorption. This is observed in facial lesions and decreases after treating with topical corticosteroids. Staining is negative in non lesional skin, unlike SLE. Light microscopy is most essential than DIF.

Presence of C1q deposits (29% of cases) implies high risk of systemic disease [67]. Deposition of immune reactants at DEJ is not specific to LE, as it is also found in other conditions such as Mixed connective tissue disorders, Porphyrias, Granuloma annulare, Amyloidosis, Psoriasis, Leprosy, etc. But, in these conditions, staining is more prominent in the walls of blood vessels and only one type of Ig class is positive. On the other hand in LE, heavy deposits involves many

immunoglobulin types in addition to complements. Serum properdin levels are increased in SLE and DLE.

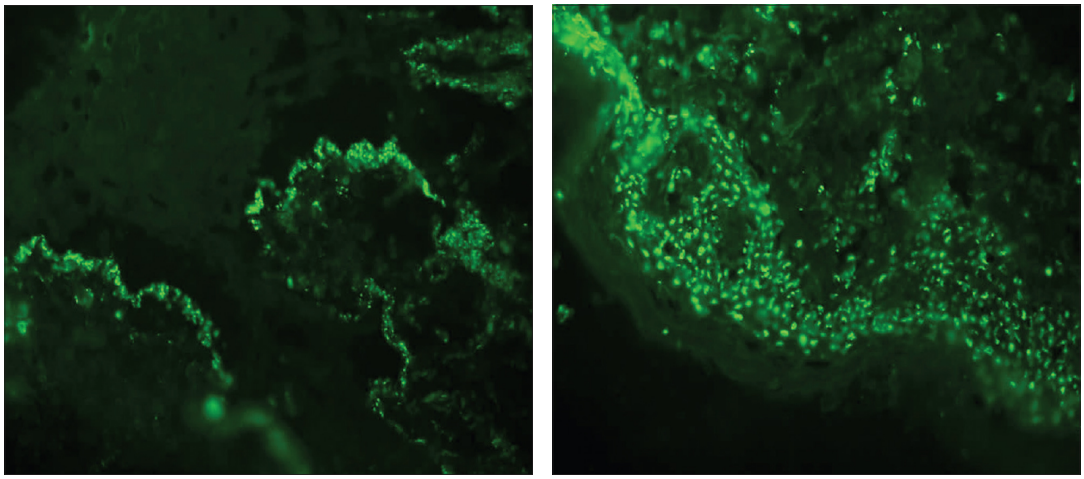


Figure 4: DIF in DLE – IgM reactive granular deposits along DEJ (anti IgM ,x400) ; IgG reactive diffuse nuclear staining in epidermal cells (antinuclear antibody in vivo) , Anti IgG, x400 [68].

LE PANNICULITIS: It shows linear staining at dermoepidermal junction

SCLE :

It shows granular pattern of immunoglobulin deposition at dermo epidermal junction, in 60% of cases, but not as thick as in DLE. Speckled pattern of fine, dust like particles of IgG is seen in cytoplasm of basal cells and dermal infiltrates. It is seen only in 3% of cases [35].

SLE: [69]

Immunoglobulins commonly IgG, less frequently IgA and IgM with complements C1 and C3 show either linear or granular deposits along the dermoepidermal junction. It is seen in 80% of patients with SLE and DLE, especially in acute lesions and in light exposed areas, whereas in early and late stages, it may be negative. SLE is associated with IgG, IgM, IgA, C4 and properdin positivity. IF staining may be homogenous or granular depending on the stage of the disease. The stippled band is found in uninvolved normal skin; linear bands in new active lesions and homogenous staining in chronic lesions.

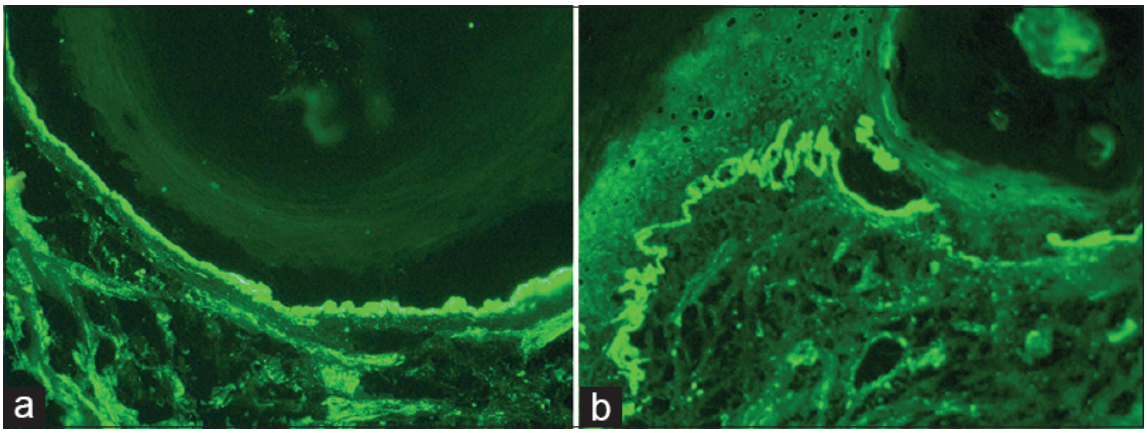


Figure 5: DIF in SLE : a) Dense continuous granular deposits of IgG along DEJ (anti IgG, x 200); b) Dense continuous granular deposits of IgA along DEJ (anti IgA, x 200) [70].

TABLE 1: LUPUS BAND TEST (LBT) OF LESIONAL AND NON LESIONAL SITES IN VARIOUS SUBTYPES OF CLE:

DISEASE	LESIONAL LBT (%)	NON LESIONAL, NON PROTECTED LBT (%)
CHRONIC DLE	60 – 90	0
SUBACUTE LE	60 – 100	0
SYSTEMIC LE	90 – 100	50 – 90

(65)

LE CELL TEST: [23]

In this test, the patient's serum mixed with white blood cells is incubated at room temperature. Then this mixture is shaken vigorously with the glass beads to expose the nuclear material. Smears made from the incubated WBCs stained with wright's stain, will show the phagocytized nuclear material inside the neutrophils, if the antinuclear antibody is present. It occurs as large, round, smoky amorphous basophilic body which compresses the nucleus against the cell membrane. This is LE cell.

IMMUNOHISTOCHEMISTRY: [72]

Lymphocytic infiltration consisting predominantly of T lymphocytes which are mixture of CD4, CD8 and HLA DR cells in all types of cutaneous LE. Vascular activation is associated with ICAM-1, E-selectin, P- selectin and vascular adhesion molecule 1.

The skin homing cytotoxic lymphocytes which expresses granzymes B, along with Th1 pattern, targets adnexal structures which helps in understanding the inflammatory process and scarring in cutaneous LE.

Identifying the target antigen is very essential in understanding the pathogenesis of DLE, along with role of TNF alpha and IL-10.

ELECTRON MICROSCOPY :

DLE and SLE lesions shows changes in lamina densa and basal cells. Changes in basal cells includes cytoplasmic vacuolization, necrosis and degeneration. Colloid or civatte bodies may be found.

DLE: Epidermis show basal layer disorganization, basement membrane reduplication and scattered apoptotic keratinocytes [35]. Dermis

show dendritic macrophages, indeterminate cells and dendritic cells with short and blunt dendrites.

SLE: Direct immunoelectron microscopy of perilesional skin in bullous SLE shows immunoreactants in continuous band like pattern below lamina densa. Early bulla formation is indicated by a separation plane in dermis, below the continuous band formed earlier.

DIFFERENTIAL DIAGNOSIS :

1. **LICHEN PLANUS:** [35]

It presents as violaceous, purple, pruritic papules and commonly involves oral cavity, flexor aspect of wrists, trunk, thighs and genitalia. Sometimes, nail and oral lesions may be the only manifestation.

HISTOPATHOLOGY :

The following histopathological findings helps to differentiate it from CLE

1. Wedge shaped hypergranulosis
2. Broad acanthosis (saw tooth appearance)
3. Band like infiltrates obscuring the dermoepidermal junction
4. Eosinophilic colloid bodies and variable melanin incontinence

5. Early lesions – increased number of langerhans cells in epidermis

The common findings include :

Hyperkeratosis, basal cell vacuolar degeneration and apoptotic keratinocytes (civatte bodies).

Hypertrophic epidermis resembles hypertrophic Lichen planus.

There is atrophy of adipose tissue with mild lymphocytic infiltrate and dermal mucin deposition in Lichen planus similar to Lupus panniculitis. Immunofluorescence and lupus band test are negative in Lichen planus.

2. **DERMATOMYOSITIS:** [35]

It is a connective tissue disorder having similar histopathological findings of systemic and subacute lupus erythematosus.

COMMON FINDINGS :

Epidermal atrophy, basal cell vacuolar degeneration, thickening of basement membrane and interstitial mucin deposition.

Lupus erythematosus in addition has hyperkeratosis, follicular plugging, periadnexal inflammatory cell infiltrates and vacuolar degeneration of outer root sheath epithelium.

IMMUNOFLUORESCENCE :

Dermatomyositis has positive staining for IgM in colloid bodies of papillary dermis. Deposition of C5b -9 (membrane attack complex) along the dermoepidermal junction and vessels are the most characteristic feature of dermatomyositis.

LUPUS BAND TEST – Negative

Plasmacytoid dendritic cells (CD 123) is found in epidermis in dermatomyositis and in dermis in case of LE. The clinical and serological datas are important to distinguish these 2 disorders.

3. POIKILODERMA ATROPHICANS VASCULARE (PAV):

Congenital LE has histological features similar to poikiloderma congenital (Rothmond Thomson Syndrome) or congenital telangiectatic erythema (Bloom's syndrome).

PAV changes can be found in LE, dermatomyositis and patch stage of mycosis fungoides. The clinical, serological and DIF findings are essential to differentiate these disorders. The usual histopathological features includes epidermal atrophy, hyperkeratosis, basal cell vacuolar degeneration, scattered dermal melanophages, rare apoptotic

keratinocytes, telengiectactic vessels and inflammatory cell infiltrates in upper dermis.

POIKILODERMATOUS LE:

It is common in sun exposed sites. Perivascular and periadnexal inflammatory infiltrates and mucin deposition in dermis favours LE.

4. SYPHILIS :

The histopathological changes in syphilis includes interface dermatitis, perifollicular inflammation and numerous plasma cells. Dermal vessels are surrounded by inflammatory infiltrates – COAT SLEEVING OF VESSELS.

Definite diagnosis is by demonstration of spirochete in tissue with silver stains (Warthin starry or steiner and steiner stains) or IHC with newer monoclonal antibodies.

LE: Periadnexal inflammation and mucin deposition in dermis.

5. POLYMORPHIC LIGHT ERUPTION :

It is a photosensitive disorder occurring in spring. The only prominent histological finding is the presence of dermal edema, which is not accompanied by mucin deposition. The histological findings of LE such

as hyperkeratosis, basement membrane thickening, follicular plugging, interface changes, basal cell vacuolar degeneration and perifollicular inflammation are not seen.

DIF and serological tests can be definitive for diagnosis.

6. CUTANEOUS LYMPHOMA / LYMPHOCYTOMA CUTIS:

It is characterized by the presence of dense lymphocytic infiltrates and atypical lymphoid cells in interstitial pattern and not around pilosebaceous structures as seen in LE. Interstitial dermal mucin may be seen. Typical epidermal changes in LE are not found.

7. MIXED CONNECTIVE TISSUE DISEASE:

It is characterized by histopathological features similar to Lupus Erythematosus along with sclerosis or hyalinization of dermal collagen, thick walled blood vessels and atrophy of adnexal structures. There may be extension of sclerosis of collagen into subcutaneous tissue.

TABLE 2: DIFFERENTIAL DIAGNOSIS OF CLE

Histopathological features	LE	Lichen planus	Dermatomyositis	PAV	Syphilis	PLE	Lymphoma
Hyperkeratosis	+	+	-	+	-	-	-
Epidermal atrophy	+	-	+	+	-	-	-
Hypergranulosis	-	+	-	-	-	-	-
Broad acanthosis	-	+	-	-	-	-	-
Basal cell degeneration	+	+	+	+	+	-	-
Follicular plugging	+	-	-	-	-	-	-
Band like infiltrates	-	+	-	-	-	-	-
Colloid bodies	+	+	-	-	-	-	-
Melanin incontinence	+	+	-	+	-	-	-
Interstitial mucin	+	-	+	-	-	-	+
Basement membrane thickening	+	-	+	-	-	-	-
Increased no of langerhans cells in epidermis	-	+	-	-	-	-	-
Periadnexal inflammation	+	-	-	-	-	-	-
Perivascular inflammation	+	-	-	-	+	+	-
Plasmacytoid dentritic cells (CD 123)	+ **(Dermis)**	-	+ **(Epidermis)**	-	-	-	-

Numerous plasma cells	-	-	-	-	+	-	-
Interstitial pattern of inflammation	-	-	-	-	-	-	+
Dermal edema	+	-	-	+	-	+	-
Immunofluorescence	+	-	**IgM,C5b-9 along DEJ and vessels**	-	-	-	-

McCright WG et al [73] studied 119 skin biopsy specimens of different types of CLE and found that though there were similar histopathological features between them, there was some considerable variation in the degree of changes.

Bangert et al [74] studied the distinguishing features between DLE and SCLE. The important features were epidermal atrophy, hyperkeratosis, basement membrane thickening, cellular infiltration and follicular plugging.

Kathleen M et al [75] studied 27 cases of CLE and stated that the most helpful clinical finding in distinguishing SCLE from DLE was non indurated, non-scarring lesions with photosensitivity. Histopathologically, there was sparse superficial lymphocytic infiltrate in SCLE compared to

dense deeper infiltrates in DLE. On DIF, 7 patients of SCLE showed epidermal IgG deposition.

Karumbaiah KP et al [76] studied 20 cases of Cutaneous LE , in which 9 were DLE, 7 were ACLE and 4 were SCLE. The common age group affected were 21- 50 years of age. Male to female ratio was approximately 1:1.9. The histopathological features between different types of LE were studied. DLE patients had features such as thickening of basement membrane and dense lymphocytic infiltrate in dermis. ACLE and SCLE patients had features like basal cell vacuolar degeneration, subepidermal edema, colloid bodies and mild dermal lymphocytic infiltrates. PAS stain showed basement membrane thickening more commonly in DLE.

Systemic Lupus Erythematosus, a prototype of autoimmune disorder is increasing in the incidence over the past few years. Clinical features are more often typical and serological tests though helpful in diagnosis are sometimes equivocal. Some clinical features have overlapping manifestations, when biopsy examination becomes mandatory.

In such cases, the histopathological features are sometimes not conclusive due to variations in the age of the lesion, site of biopsy and atypical presentations. The purpose of this study is to review these histopathological features and find out the most commonly occurring findings and also to study the role of special stains like Periodic acid Schiff with Alcian blue in highlighting the basement membrane thickening and interstitial mucin deposition in our hospital setting, as such studies have not been done often.

MATERIALS AND METHODS

STUDY DESIGN:

The present study is a prospective study conducted in department of Pathology during the period of January 2017 to June 2018. Ethical committee clearance was obtained on 21-12-2016.

STUDY PERIOD: January 2017 to June 2018

INCLUSION CRITERIA:

1. All patients with clinically diagnosed isolated CLE or SLE having cutaneous manifestations.
2. All ages and both sexes.

EXCLUSION CRITERIA:

1. Treated patients of LE.
2. Patients of LE with non-specific skin manifestations.
3. Pregnancy.

PROCEDURE :

In patients with clinically suspected and diagnosed CLE, 5mm punch biopsy was taken in Dermatology department, CMCH. The specimens were received in the Pathology department in a container, containing 10% Neutral buffered formalin.

The specimen was fixed in formalin for 12 to 24 hours and subjected to routine processing and embedding. The skin biopsy specimen was oriented perpendicular to the cutting surface , so that all the layers are properly visualized. 4 slides, each containing 3 to 4 sections of about 3-4 microns thickness were prepared. Later, they were stained with haematoxylin and eosin stain and also with PAS with alcian blue.

HEMATOXYLIN AND EOSIN STAINING METHOD:

REAGENTS USED:

1. Hematoxylin solution – Erhlich's hematoxylin
2. Eosin Y 1% solution
3. Acid alcohol 1% solution

PROCEDURE:

1. The sections were deparaffinized in xylene by immersing for 30 seconds.
2. The sections were placed in Isopropyl alcohol for 15 minutes and washed in running tap water.
3. Then the sections were stained in Erhlich's hematoxylin for 10 to 15 minutes.
4. Differentiation was done with 1% acid alcohol – two to three dips.
5. Blueing was carried out for 10 minutes.
6. Then the sections were counterstained with eosin 1% solution – 3 to 4 dips and washed in running tap water.
7. The sections were air dried and mounted with DPX and cover slip.

SPECIAL STAIN :

PERIODIC ACID SCHIFF WITH ALCIAN BLUE STAIN:

The special stains were performed in histologically diagnosed CLE patients, to look for thickening of basement membrane and interstitial mucin deposition in dermis.

PAS STAIN: [77]

It is the most commonly used technique to demonstrate carbohydrates or glycol conjugates. It is useful in distinguishing glycogen and mucin. It is helpful in assessing the basement membrane thickness, due to reactivity of Schiff reagent with glycoproteins present in the basal lamina.

PRINCIPLE :

It is based on the mechanism of free aldehyde groups in carbohydrates reacting with the Schiff reagent to form magenta / bright red colored product.

The initial steps involved are oxidation of hydroxyl groups (1,2 glycols) in carbohydrates, leading to formation of 2 free aldehyde groups and the adjacent carbon to carbon bond is cleaved. The oxidation is brought about by the periodic acid (HIO4) of 0.5 -1% for 5 to 10 minutes.

Then the aldehyde groups react with Schiff reagent to form the coloured product. The intensity of colour depends on concentration of reactive glycol structures in tissues.

CELLS AND COMPONENTS POSITIVE FOR PAS:

- Glycogen, starch
- Mucin (sialomucin ,neutral mucin)
- Basement membrane, reticulin
- Fungi, alpha antitrypsin
- Thyroid colloid, Russell bodies
- Corpora amylacea

ALCIAN BLUE STAIN:

It is a compound consisting of copper containing phthalocyanine ring, which is linked to 4 isothiouranium groups through thioether bonds. The cationic isothiouranium groups react with polyanionic molecules in tissue through electrostatic linkages. Alcian blue at a ph of 2.5 is very essential.

COMBINED PAS WITH ALCIAN BLUE STAIN :

It is done to differentiate acidic from neutral mucin, which is stained by alcian blue and also to demonstrate the basement membrane thickness with PAS.

After overnight incubation, bring the sections to water.

SECTIONS TO WATER :

1. Sections were deparaffinized with xylene for 3 times of 10 minutes each.

2. Then the sections were dehydrated with absolute alcohol of 2 changes, 5 minutes each.

3. Sections were then washed in tap water for 5 minutes

4. Later, the slides were rinsed with distilled water for 2 minutes.

STAINING TECHNIQUE:

- The slides were stained with alcian blue solution (ph 2.5) for 30 minutes and washed with running tap water for 5 minutes
- Then rinsed in distilled water
- Sections were oxidized with 1% aqueous periodic acid for 10 minutes
- Washed in tap water for 5 minutes and stained with

  Schiff reagent for 15 minutes
- Again washed in running tap water for 10 minutes
- Stained with haematoxylin solutions for 2 minutes.
- Washed in running tap water for 5 to 10 minutes (till blueing)

- Then rinsed in tap water for 5 minutes
- Sections were dried and mounted with DPX and cover slip

RESULTS :

- Basement membrane –magenta /bright red
- Acid mucin – blue
- Neutral mucin – magenta
- Nuclei – pale blue

HISTOPATHOLOGICAL EXAMINATION:

The following histological features were observed in hematoxylin and eosin stained slides.

1. Hyperkeratosis with follicular plugging
2. Epidermal atrophy and colloid bodies (apoptotic keratinocytes).
3. Liquefactive or vacuolar degeneration of the basal cell layer – vacuolar space between and beneath the basilar keratinocytes.
4. Basement membrane thickening
5. Periadnexal and perivascular inflammatory infiltrates.

Additional findings if any, were also observed.

Later, PAS with Alcian blue stain were carried out to demonstrate the intensity of basement membrane thickening and the amount and location of mucin deposition.

Finally the various histological findings with clinical features were correlated and tabulated to observe the results.

1. Incidence and frequency of various types of CLE.
2. Age and gender distribution.
3. Site of involvement
4. Cutaneous manifestations
5. Common histopathological findings in various subtypes of CLE.
6. Basement membrane thickening and mucin deposition in special stain.

OBSERVATION AND RESULTS

This is a prospective study which includes 40 cases of CLE of which 19% were ACLE, 6% SCLE and 15% DLE. All these cases were stained with hematoxylin and eosin stain and PAS with Alcian blue. Treated cases were not included in the study.

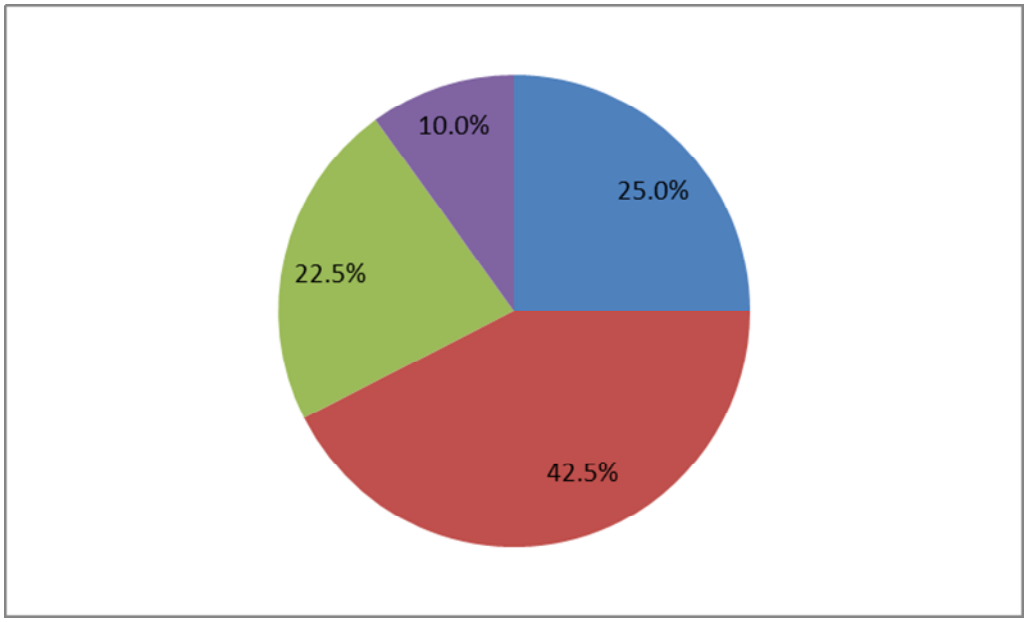
TABLE 3: MEAN AGE OF THE STUDY

	N	Minimum	Maximum	Mean ± SD
AGE	40	17.0	75.0	41.075 ± 14.1

TABLE 4: AGE DISTRIBUTION OF CLE

Age in years	Frequency	Percent
16-30	10	25.0
31-45	17	42.5
46-60	9	22.5
>61	4	10.0
Total	40	100.0

CHART 1: AGE DISTRIBUTION OF CLE

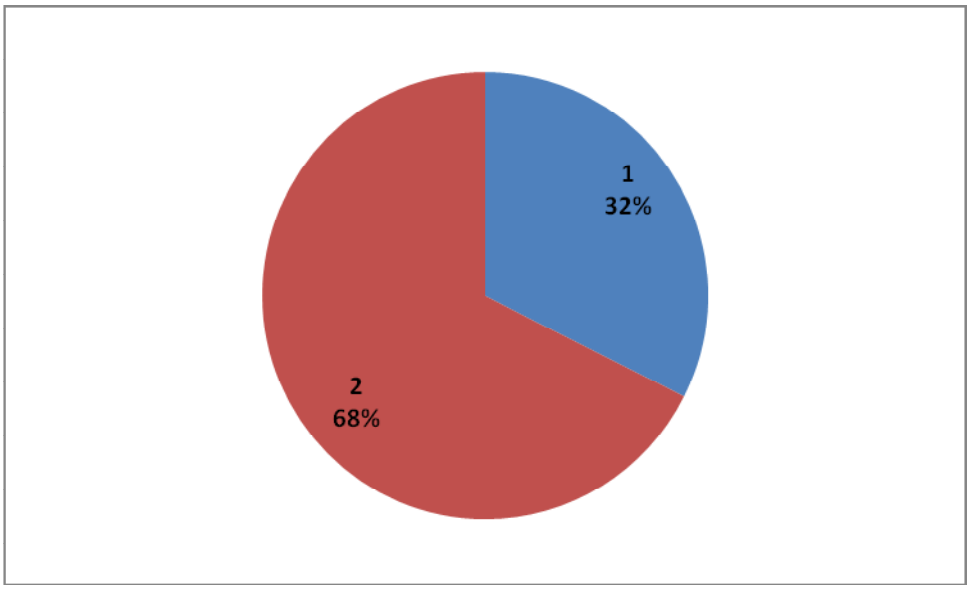


The mean age of occurrence was 41 years and ranged between 17 to 75 years of age. 42.5% of the cases were between 31 -45 years. (i.e peak age of occurrence), followed by 16- 30 years of age group.

TABLE 5: GENDER DISTRIBUTION OF CLE

Gender	Frequency	Percent
Male	13	32.5
Female	27	67.5
Total	40	100.0

CHART 2: GENDER DISTRIBUTION OF CLE

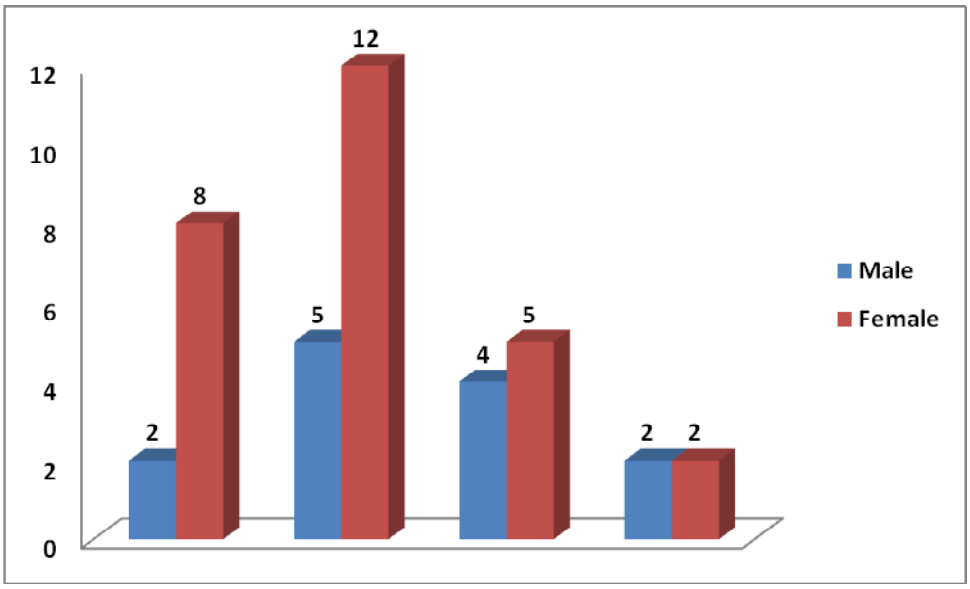


As per the present study, of the 40 cases of CLE, 27 cases (67.5%) were females and 13 (32.5%) were males. Female to male ratio is 2:1.

TABLE 6: GENDER DISTRIBUTION AMONG DIFFERENT AGE GROUPS IN THE STUDY

Age in years	Male	Female
16-30	2(20.0%)	8(80.0%)
31-45	5(29.4%)	12(70.6%)
46-60	4(44.4%)	5(55.6%)
>61	2(50.0%)	2(50.0%)
Total	13(32.5.0%)	27(67.5%)

CHART 3: GENDER DISTRIBUTION AMONG DIFFERENT AGE GROUPS IN THE STUDY

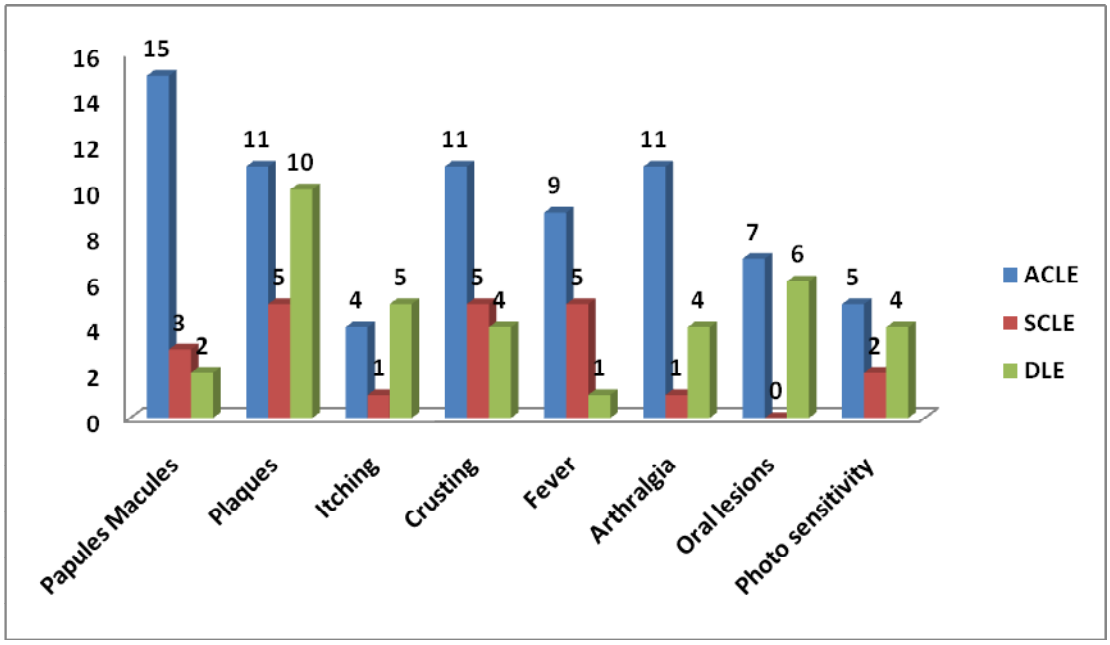


Among the females, the peak age of occurrence was between 31 -45 years (70.6%), which is similar to males (29.4%).

TABLE 7: CLINICAL FEATURES OF CLE

	Papules & Macules	Plaques	Itching	Crusting	Fever	Arthralgia	Oral lesions	Photo sensitivity
ACLE (19)	15 (78.9%)	11 (57.9%)	4 (21.1%)	11 (57.9%)	9 (47.4%)	11 (57.9%)	7 (36.8%)	5 (26.3%)
SCLE (6)	3 (50.0%)	5 (83.3%)	1 (16.7%)	5 (83.3%)	5 (83.3%)	1 (16.7%)	0 (0.0%)	2 (33.3%)
DLE (15)	2 (13.3%)	10 (66.7%)	5 (33.3%)	4 (26.7%)	1 (16.7%)	4 (26.7%)	6 (40.0%)	4 (26.7%)

CHART 4: CLINICAL FEATURES OF CLE

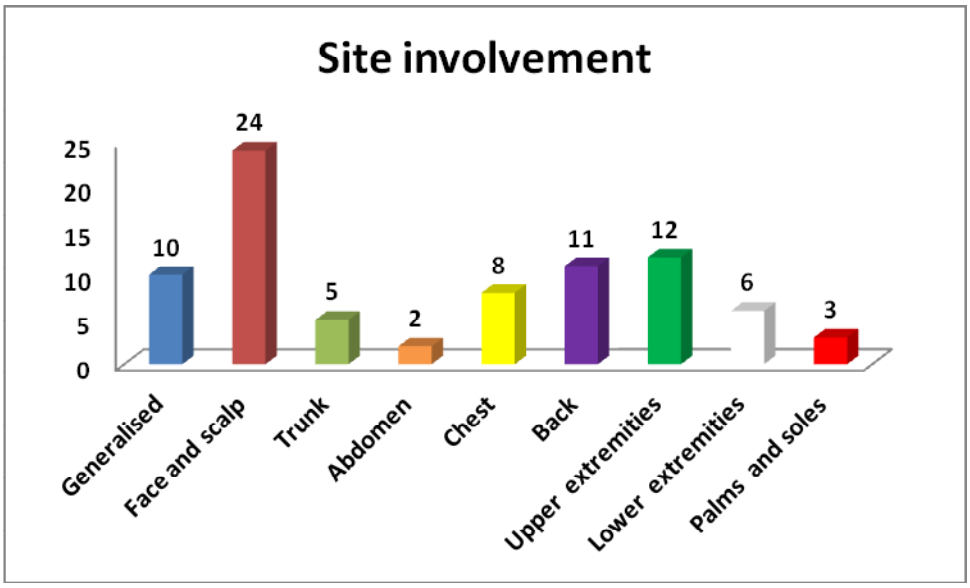


In acute lesion, the incidence of maculopapular lesion was relatively higher. In SCLE and DLE, plaque like lesions were relatively higher. Arthralgia was more often observed in patients with ACLE and oral lesions were equally common in ACLE and DLE. Photosensitivity reactions were equally common in ACLE and DLE (27%).

TABLE 8: SITE INVOLVEMENT IN CLE

Sites	No. of cases	Percentage (%)
Generalised	10	25
Face and scalp	24	60
Trunk	5	12.5
Abdomen	2	5
Chest	8	20
Back	11	27.5
Upper extremities	12	30
Lower extremities	6	15
Palms and soles	3	7.5

CHART 5 : SITE INVOLVEMENT IN CLE

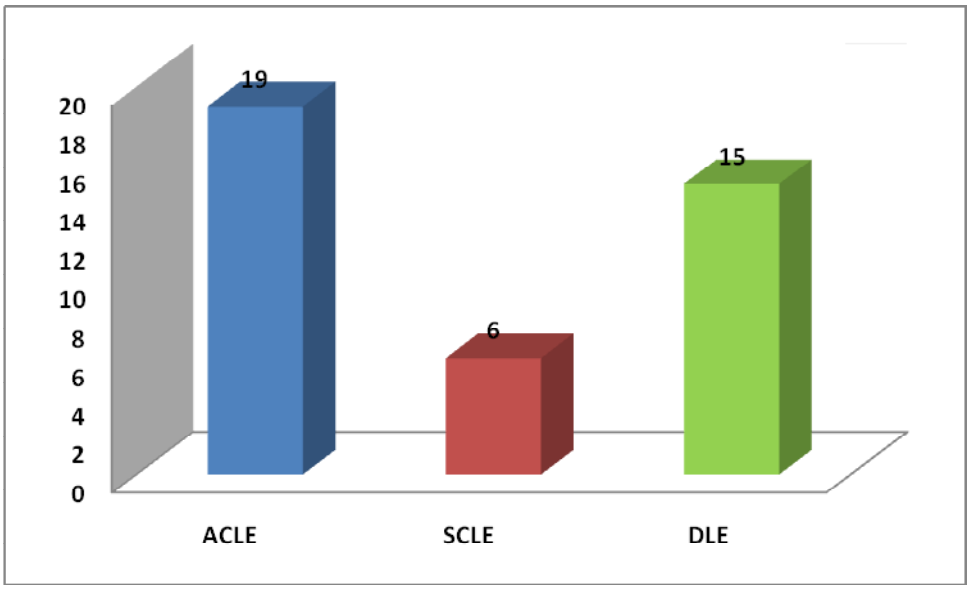


In the present study, generalised involvement was observed in 10 cases (25%). Face and scalp were most commonly involved (60% of cases), followed by back and upper extremities. Palms and soles were affected in 3 cases, comprising 7.5%.

TABLE 9: PATHOLOGICAL DIAGNOSIS IN THE STUDY

Pathological diagnosis	Frequency	Percent
ACLE	19	47.5
SCLE	6	15.0
DLE	15	37.5
Total	40	100.0

CHART 6: PATHOLOGICAL DIAGNOSIS IN THE STUDY

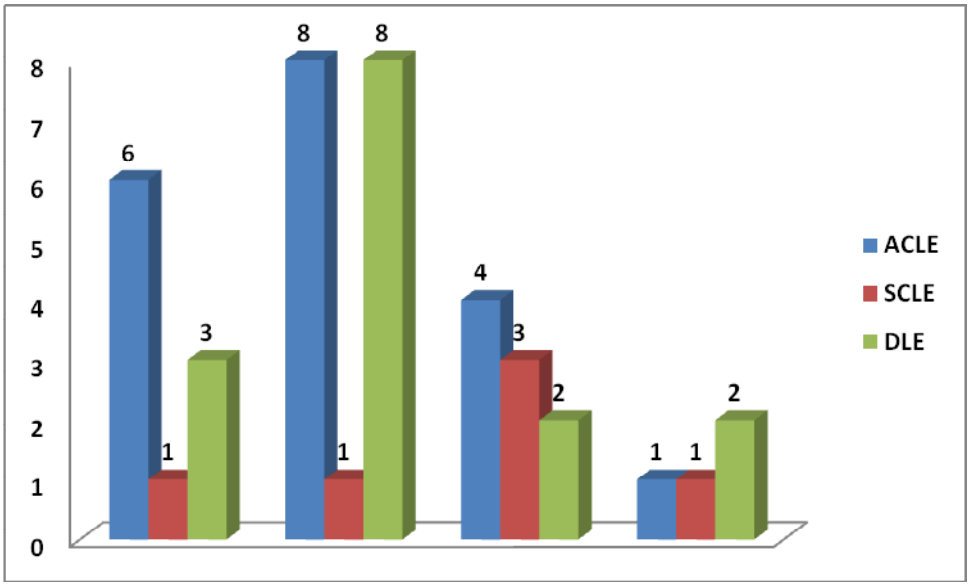


In our study, the most common subtype diagnosed was Acute LE (ACLE), which constitutes 47.5% of cases, followed by DLE (37.5%) and SCLE (15%).

TABLE 10: PATHOLOGICAL DIAGNOSIS AMONG DIFFERENT AGE GROUPS IN THE STUDY

Age in years	ACLE	SCLE	DLE
16-30	6(60.0%)	1(10.0%)	3(10.0%)
31-45	8(47.1%)	1(5.9%)	8(47.1%)
46-60	4(44.4%)	3(33.3%)	2(22.2%)
>61	1(25.0%)	1(25.0%)	2(50.0%)

CHART 7: PATHOLOGICAL DIAGNOSIS AMONG DIFFERENT AGE GROUPS IN THE STUDY

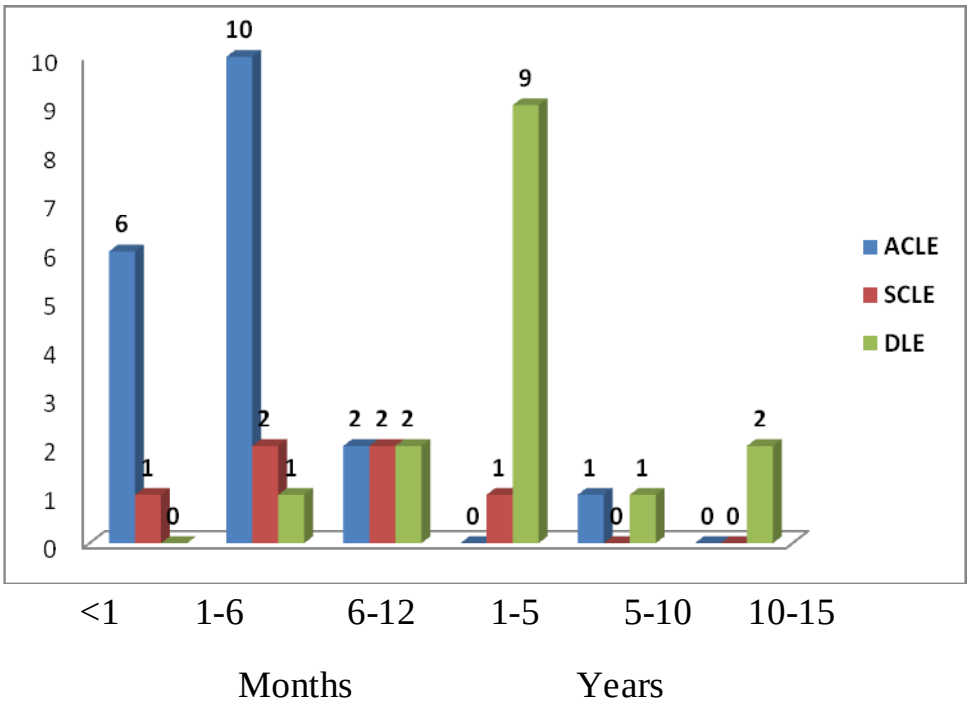


Acute lesions were most commonly seen in between 31-45 years of age. DLE was also most common between 31-45 years of age and SCLE was common between 46 -60 years.

TABLE 11: PATHOLOGICAL DIAGNOSIS WITH DURATION OF SYMPTOMS IN THE STUDY

Duration	ACLE	SCLE	DLE
< 1 month	6(85.7%)	1(14.3%)	0(0.0%)
1-6 months	10(76.9%)	2(15.4%)	1(7.7%)
6-12 months	2(33.3%)	2(33.3%)	2(33.3%)
1-5 years	0(0.0%)	1(10.0%)	9(90.0%)
5-10 years	1(50.0%)	0(0.0%)	1(50.0%)
10-15 years	0(0.0%)	0(0.0%)	2(100.0%)

CHART 8: PATHOLOGICAL DIAGNOSIS WITH DURATION OF SYMPTOMS IN THE STUDY

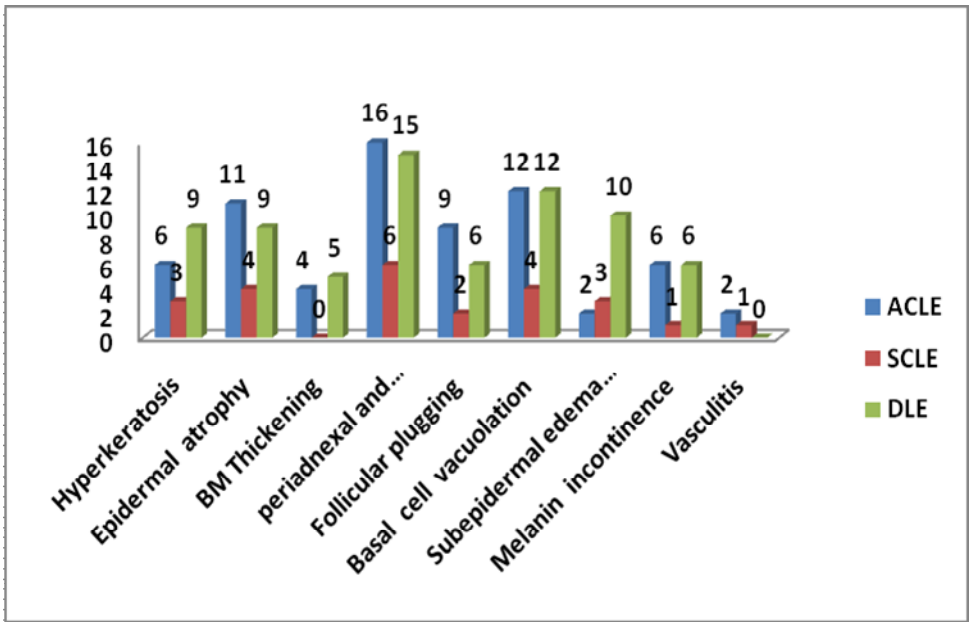


In the present study, patients with acute subtype had lesions of less than 6 months duration. DLE cases had skin lesions of 1-5 years of duration and SCLE cases had lesions between 1 to 12 months of duration.

TABLE 12: HISTOPATHOLOGICAL FEATURES OF VARIOUS SUBTYPES OF CLE

	ACLE (19)	SCLE (6)	DLE(15)
Hyperkeratosis	6	3	9
Epidermal atrophy	11	4	9
BM Thickening	4	0	5
Periadnexal and perivascular inflammation	16	6	15
Follicular plugging	9	2	6
Basal cell vacuolation	12	4	12
Subepidermal edema and dermal mucin	2	3	10
Melanin incontinence	6	1	6
Vasculitis	2	1	0

CHART 9: HISTOPATHOLOGICAL FEATURES OF VARIOUS SUBTYPES OF CLE



The most common observed histopathological feature was basal cell vacuolar degeneration, which was observed in 12 out of 19 cases of ACLE, 12 out of 15 cases of DLE and 4 out of 6 cases of SCLE.

Dermal mucin was observed most commonly in DLE. Vasculitis was more commonly seen in ACLE. The second most common finding was periadnexal inflammation, followed by epidermal atrophy, follicular plugging and hyperkeratosis.

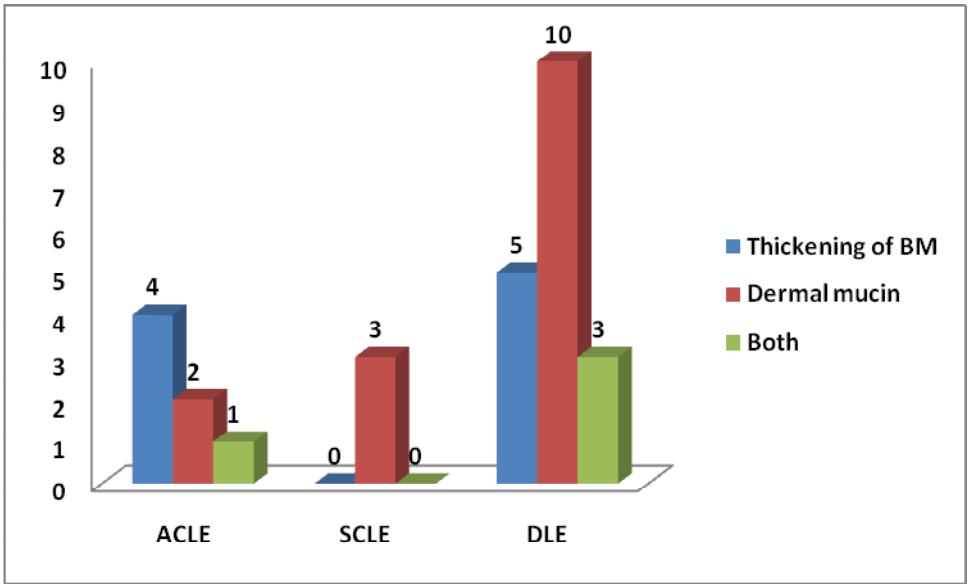
TABLE 13: SPECIAL STAIN APPLICATION

(PAS WITH ALCIAN BLUE)

	ACLE(19)	SCLE(6)	DLE(15)
Thickening of BM	4(21.1%)	0(0.0%)	5(33.3%)
Dermal mucin	2(10.5%)	3(33.3%)	10(66.7%)
Both	1(5.2%)	0(0.0%)	3(20.0%)

CHART 10: SPECIAL STAIN APPLICATION

(PAS WITH ALCIAN BLUE)



In this study, with PAS and Alcian blue stain, thickening of basement membrane was observed in 20-30% of CLE patients and dermal mucin was noted more often in DLE (66.7%). All the 6 cases of SCLE did not show basement membrane thickening.

COLOUR PLATES – MICROSCOPY

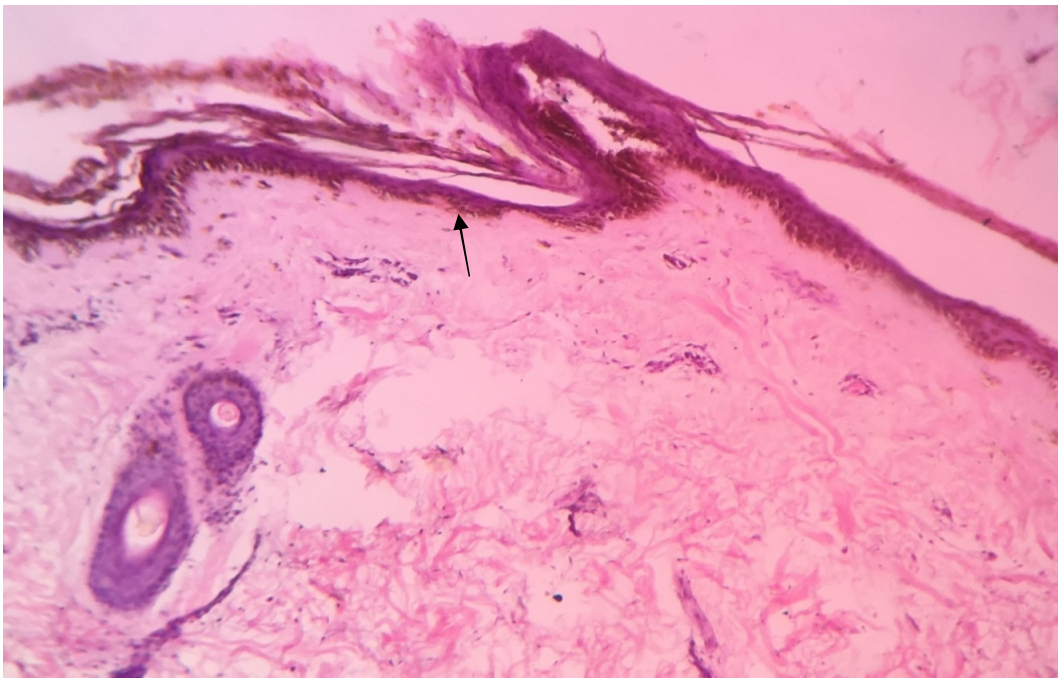


Figure 6: H & E section showing epidermal atrophy (arrow) and follicular plugging - Low power (100X).

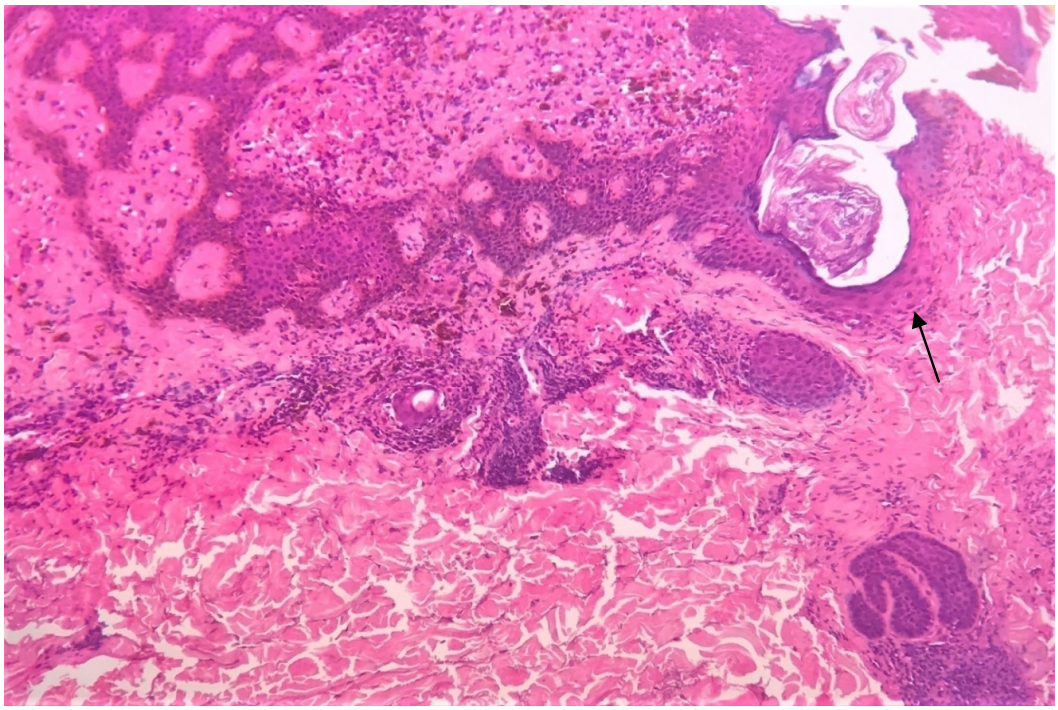


Figure 7: H & E section showing follicular plugging (arrow) with periadnexal and perivascular inflammation – Low power (100X).

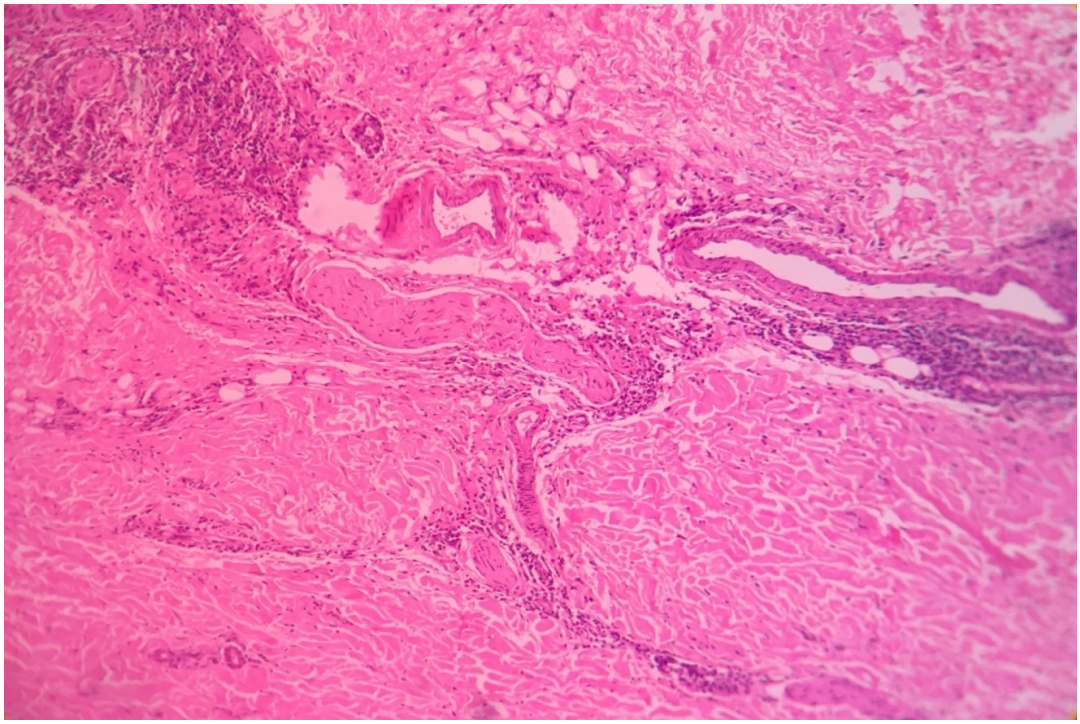


Figure 8: H & E section showing periadnexal and perivascular inflammation scanner (40X).

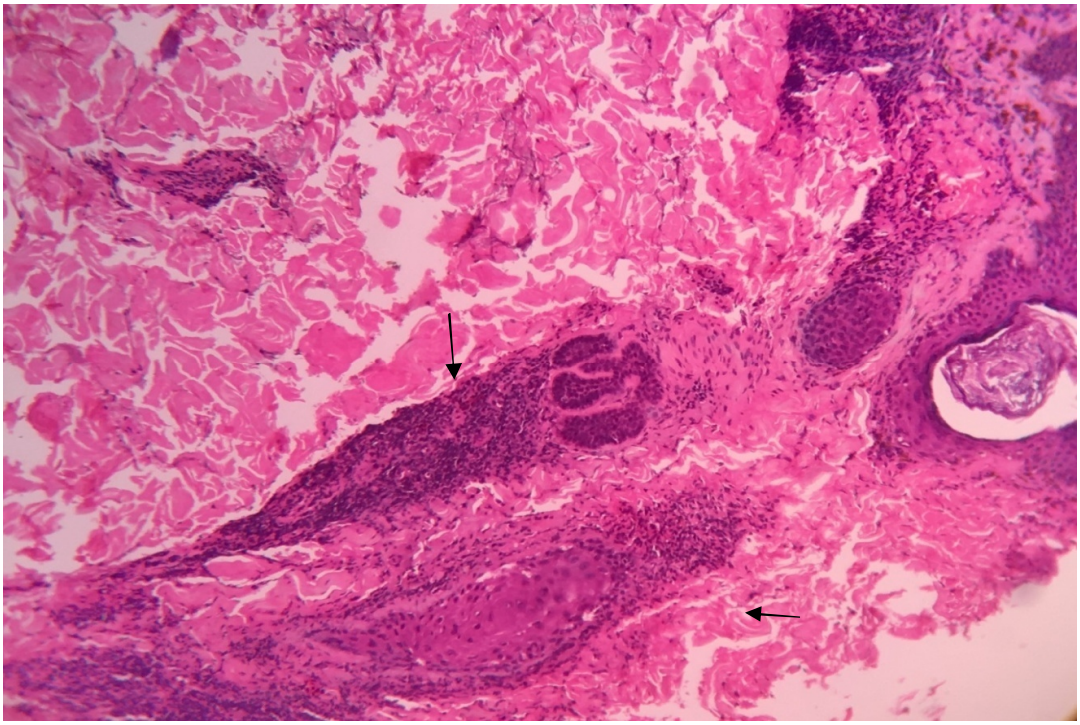


Figure 9: H & E section showing follicular plugging and periadnexal inflammation (arrow) – Low power (100X).

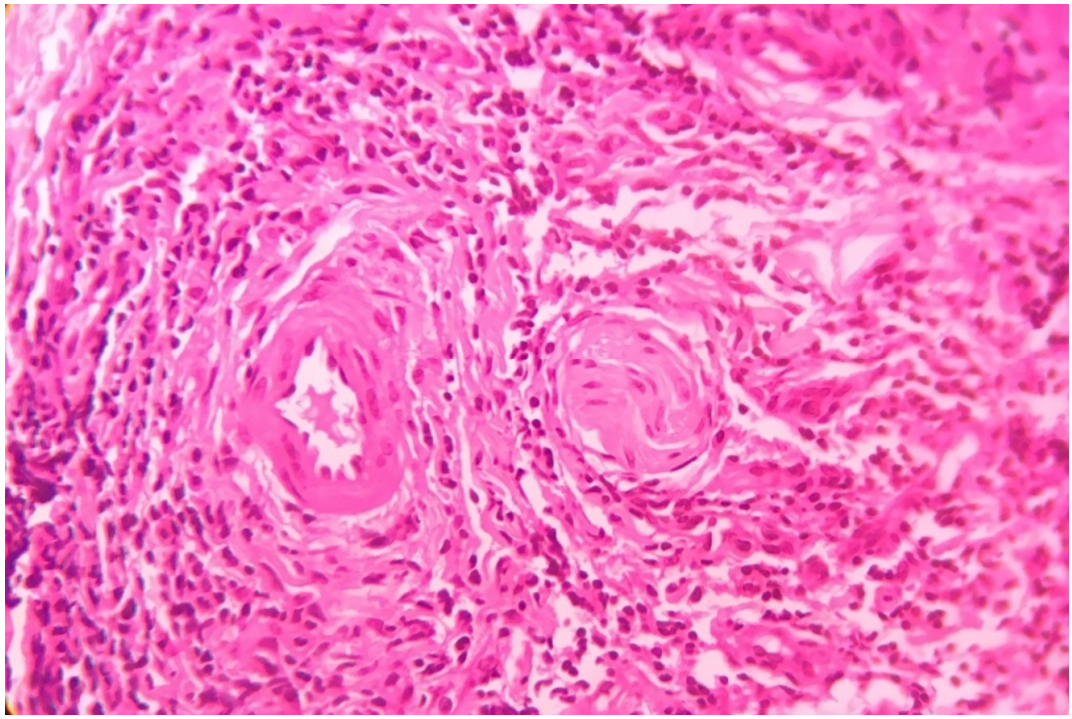


Figure 10: H & E section showing perivascular and periadnexal inflammation High power (400X).

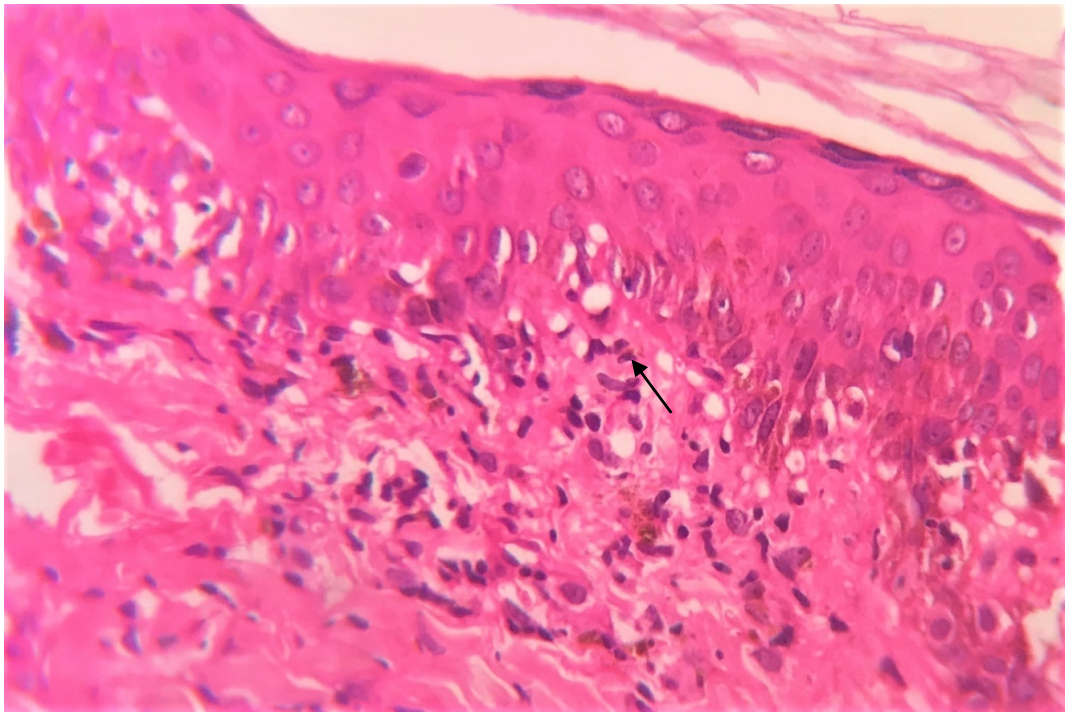


Figure 11: H & E section showing basal cell vacuolar degeneration (arrow) High power (400X).

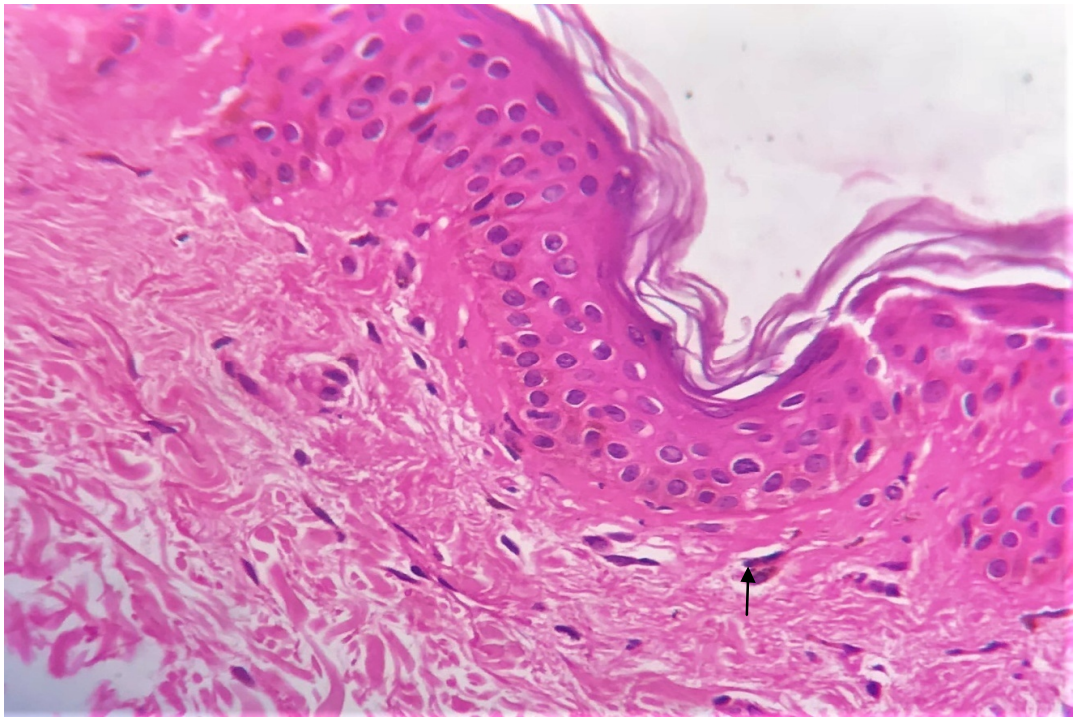


Figure 12: H & E section showing hyperkeratosis and basement membrane thickening (arrow) – High power (400X).

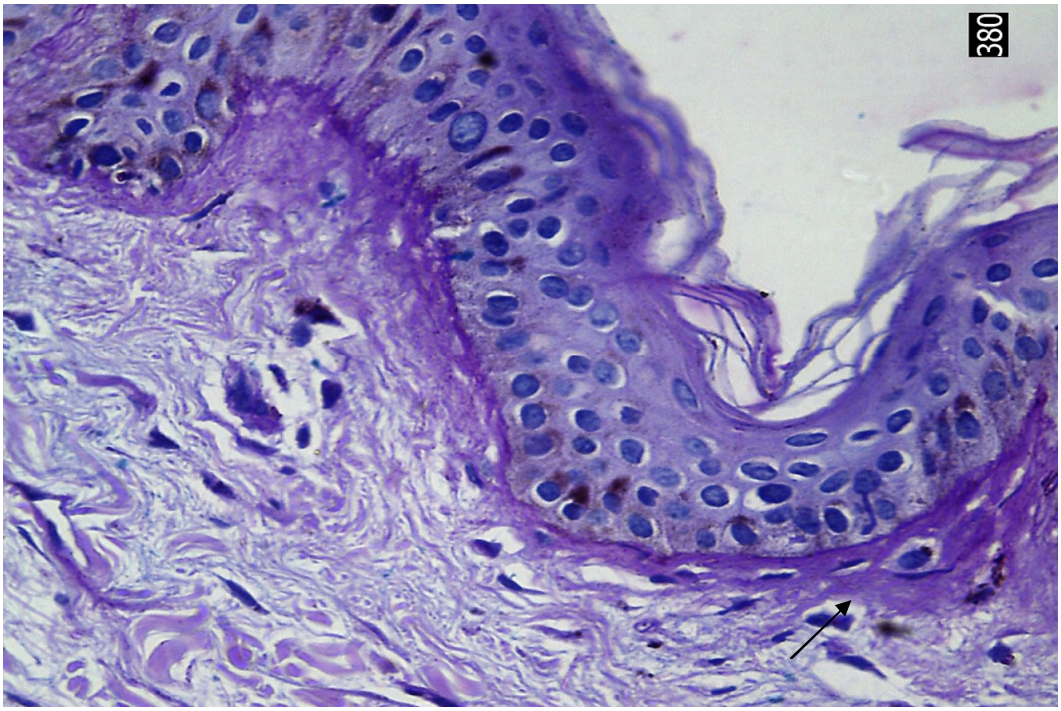


Figure 13: PAS with Alcian blue stain showing basement membrane thickening (arrow) High power (400X).

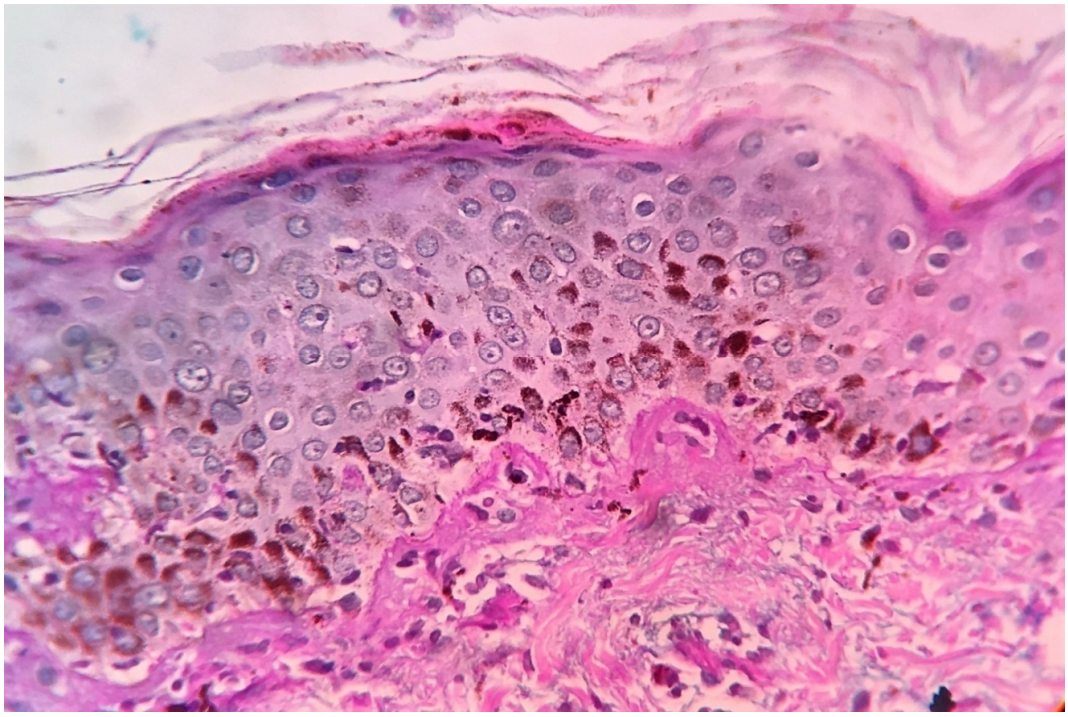


Figure 14: PAS with Alcian blue stain showing hyperkeratosis with focal basement membrane thickening and basal cell degeneration - High power (400X).

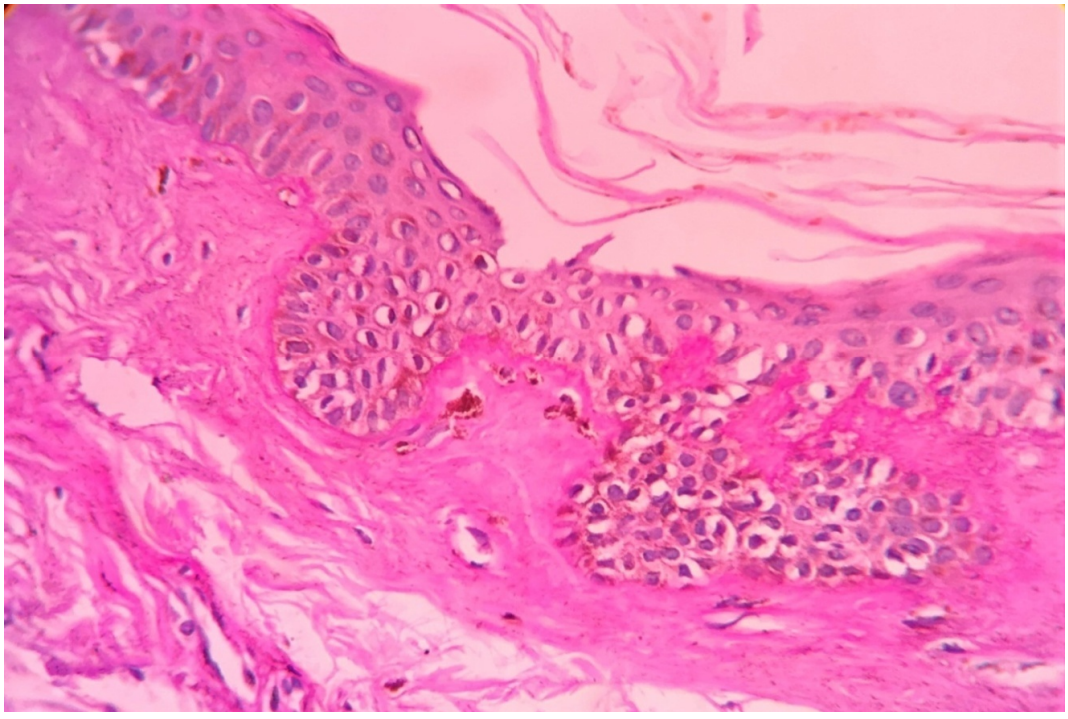


Figure 15 : PAS with Alcian blue stain showing basal cell vacuolar degeneration and mild basement membrane thickening –High power (400X).

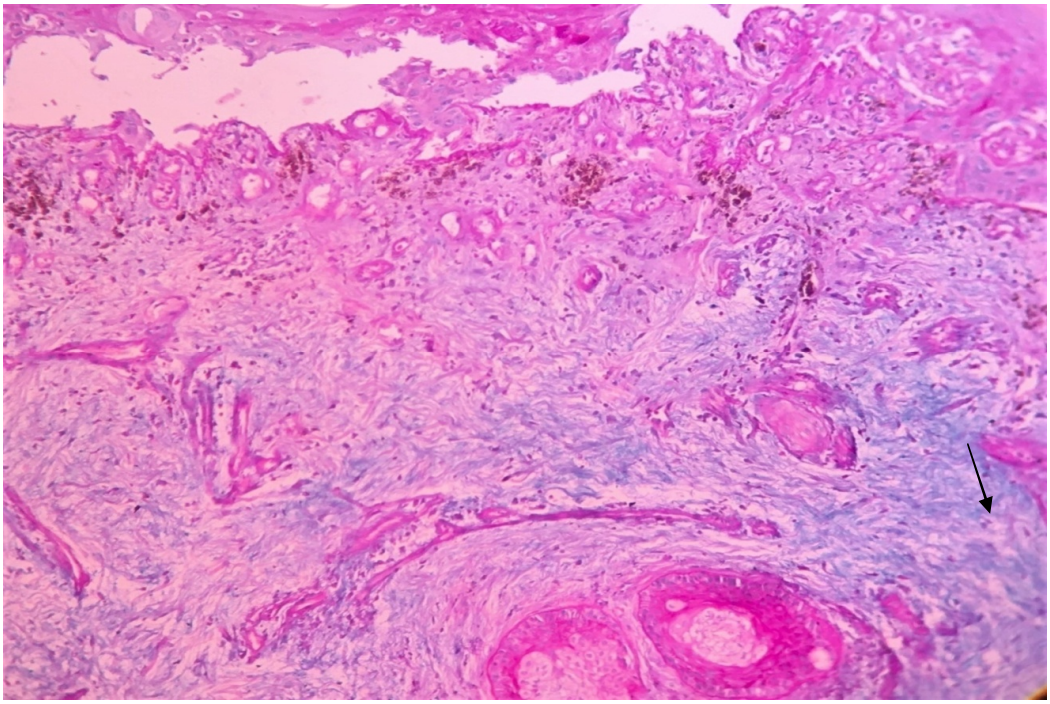


Figure 16: PAS with Alcian blue stain showing interstitial dermal mucin (arrow) Low power (100X).

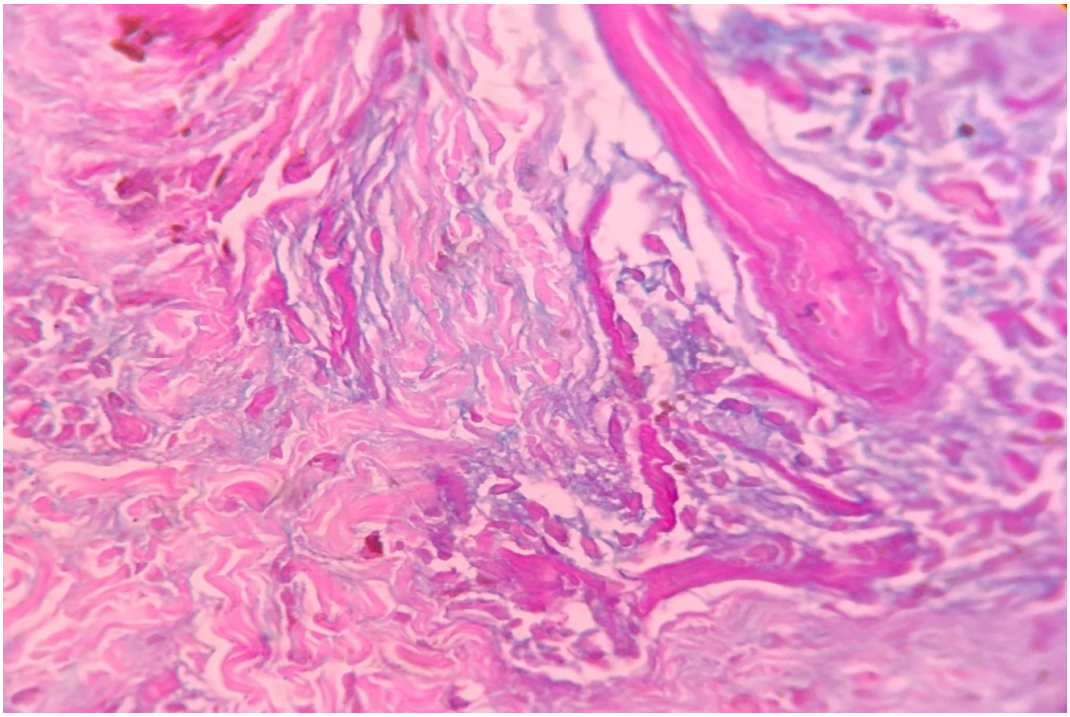


Figure 17: PAS with Alcian blue stain showing interstitial dermal mucin High power (400X).

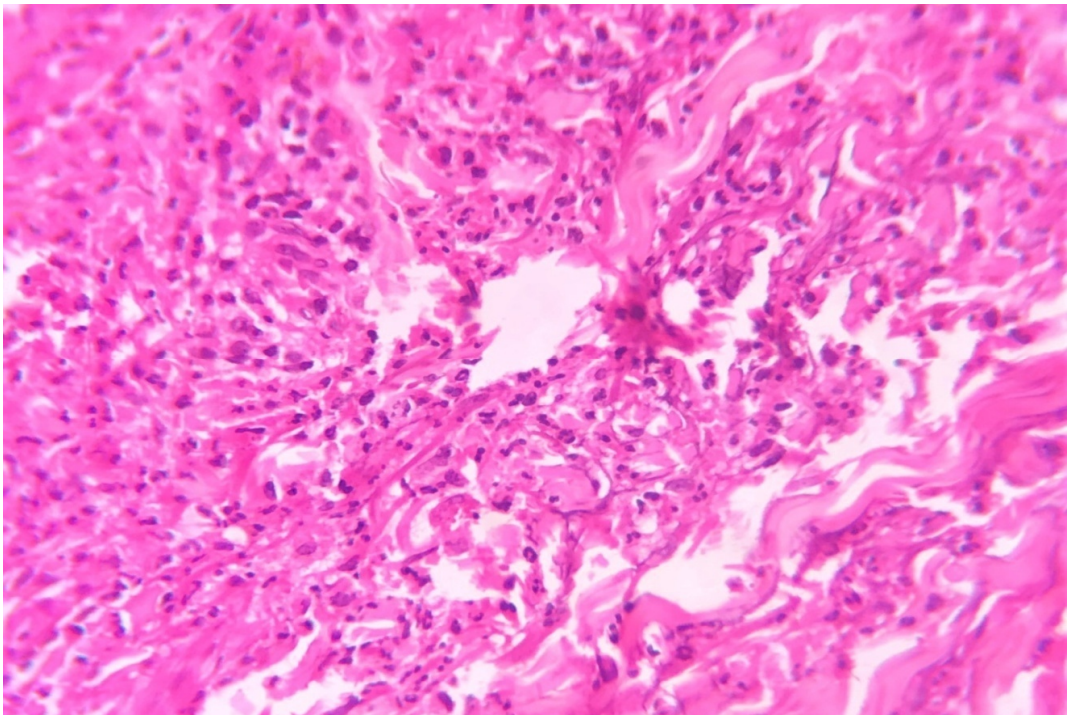


Figure 18 : H & E section showing vasculitis – High power (400X).

DISCUSSION

Connective tissue disorders, present with cutaneous lesions, the biopsy of which is useful in diagnosis and subclassification of the disease. Lupus Erythematosus is one such disorder which manifests with different skin lesions.

This prospective study was based on clinical features and the spectrum of histopathological findings in different subtypes of Cutaneous Lupus Erythematosus. The results obtained were analyzed and compared with literature based on epidemiological, clinical and histological features.

In our study, the biopsy samples of 40 patients clinically diagnosed as CLE were studied in the Department of Pathology, over a period of one and a half years, of which 19 (47.5%) patients were diagnosed as ACLE, 6 (15%) as SCLE and 15 (37.5%) as DLE. Karumbaiah et al [(76)] and Kathleen M et al [(75)] demonstrated that DLE was the most common type. In our study, ACLE was the most common subtype observed.

AGE: The peak age of occurence was between 31- 45 years of age in our study. According to Karumbaiah et al [(76)], the age group was 21 to 50 years.

Aviles- Izquierdo et al [78], demonstrated that ACLE patients were younger, compared to SCLE and CCLE. In our present study, we observed that the age of onset of ACLE was between 16 to 45 years.

Biazer et al [79] observed that the mean age at disease onset in SCLE, was higher than in patients with ACLE. We had similar results in our study.

GENDER: In our series, females (67.5%) were more commonly affected than males (32.5%), with female to male ratio is 2 :1, in comparing to Gronhagen CM et al study [80], in which female to male ratio was observed to be 3:1. In our study 31 to 45 years of females were most commonly affected.

CLINICAL FEATURES: In acute lesion, the incidence of maculopapular lesion was relatively higher. In SCLE and DLE, plaque like lesions were relatively higher similar to David et al and Griffiths et al. Arthralgia was more often observed in patients with ACLE and oral lesions were equally common in ACLE and DLE. Photosensitivity reactions were equally common in ACLE and DLE (27%). Crusting was most commonly observed in ACLE. In 30% of ACLE and DLE cases, itching was present.

SITE OF INVOLVEMENT: In this study, 60% of patients had face and scalp lesions, followed by upper extremities (30%), back (27.5%) and generalized body involvement (25%). Vera Recabarren et al[81] demonstrated that cutaneous lesions show similar distribution.

DURATION: In our present study, patients with acute subtype had lesions of less than 6 months duration. SCLE patients had lesions between 1 to 12 months of duration and DLE had skin lesions of 1 to 5 years of duration. In other studies, the duration of the symptoms with various subtypes were not mentioned.

TABLE 14: COMPARISON OF HISTOPATHOLOGICAL FEATURES OF ACLE WITH KARUMBAIAH ET AL STUDY:

HISTOPATHOLOGICAL FEATURES	KARUMBAIAH ET AL [76] – 7 CASES	PRESENT STUDY 19 CASES
Hyperkeratosis	3	6
Epidermal atrophy	4	11
Basement membrane thickening	-	4
Periadnexal and perivascular inflammation	6	16
Follicular plugging	6	9
Basal cell vacuolation	7	12
Subepidermal edema	6	2
Melanin incontinence	3	6
Vasculitis	-	2

Basal cell vacuolation and mild periadnexal and perivascular inflammation was observed in most of the cases, followed by epidermal atrophy and follicular plugging. Subepidermal edema was more common in Karumbaiah et al study [76], when compared to our study.

In our study, vasculitis was found in 2 out of 19 cases, but was not included in the above study. Basement membrane thickening was found in 4 (21.5%) cases, which was not observed in any of the cases in the above mentioned study.

TABLE 15: COMPARISON OF HISTOPATHOLOGICAL FEATURES OF SCLE IN VARIOUS STUDIES:

HISTOPATHOLOGICAL FEATURES	KARUMBAIAH ET AL [76] – 4 CASES	BANGERT ET AL [74] – 12 CASES	PRESENT STUDY – 6 CASES
Hyperkeratosis	2	12	3
Epidermal atrophy	2	10	4
Basement membrane thickening	1	8	-
Periadnexal and perivascular inflammation	4	12	6
Follicular plugging	3	2	2
Basal cell vacuolation	3	8	4
Subepidermal edema	3	3	3
Dermal mucin	-	-	3
Melanin incontinence	-	-	1
Vasculitis	-	-	1

In our series of patients, 6 cases were diagnosed to be SCLE. Basal cell vacuolar degeneration, epidermal atrophy and periadnexal and perivascular inflammation were commonly observed findings in our

study. The less common findings were hyperkeratosis, follicular plugging and subepidermal edema.

This coincides with Karumbaiah et al and Bangert et al studies. Basement membrane thickening was not identified in any of the cases in our study, which contradicts with Bangert et al study, in which 8 out of 12 cases, demonstrated thickening of basement membrane. Dermal mucin was observed in 3 out of 6 cases in our study, which was not included in the above studies mentioned.

TABLE 16: COMPARISON OF HISTOPATHOLOGICAL FEATURES OF DLE IN VARIOUS STUDIES:

HISTOPATHOLOGICAL FEATURES	KARUMBAIAH ET AL [76] – 9 CASES	BANGERT ET AL [74] – 26 CASES	PRESENT STUDY – 15 CASES
Hyperkeratosis	5	26	9
Epidermal atrophy	3	11	9
Basement membrane thickening	9	19	5
Periadnexal and perivascular inflammation	9	26	15
Follicular plugging	5	14	6
Basal cell vacuolation	7	19	12
Subepidermal edema	3	3	4
Dermal mucin	-	-	10
Melanin incontinence	-	-	6
Vasculitis	-	-	-

Basement membrane thickening was the most common feature observed in DLE in studies conducted by Karumbaiah et al and Bangert et al, which corroborates with our study. The intensity of periadnexal and perivascular inflammatory infiltrates was maximum in DLE. Dermal mucin was also commonly found in DLE patients of our study, which was not mentioned in other studies. The other features included were basal cell vacuolation, epidermal atrophy, hyperkeratosis and follicular plugging

COMPARISON OF ACLE AND SCLE IN PRESENT STUDY :

The common histopathological changes found in ACLE were basal cell vacuolar degeneration, periadnexal and perivascular inflammation and epidermal atrophy similar to that of SCLE but with lesser degree of inflammation in ACLE. Follicular plugging was found only in 2 cases of SCLE, which was less frequent than ACLE. Basement membrane thickening was not observed in any of the cases of SCLE in contrast to ACLE, whereas subepidermal edema and mucin deposition were frequently observed in SCLE than ACLE, in contrast to Karumbaiah et al study. Vasculitis was commonly found in ACLE.

COMPARISON OF SCLE AND DLE IN PRESENT STUDY :

The frequently observed histological features in DLE were basal cell vacuolar degeneration, subepidermal edema, dermal mucin followed by epidermal atrophy, hyperkeratosis and less commonly follicular plugging and basement membrane thickening but are more compared to SCLE. Dermal mucin and thickening of basement membrane were frequently observed in DLE than SCLE, similar to Karumbaiah et al study.

The combination of basal cell vacuolar degeneration and epidermal atrophy with clinical correlation are highly suggestive of SCLE, similar to Karumbaiah et al study.

SPECIAL STAIN :

Basement membrane thickening demonstrated by PAS was observed most commonly in DLE, comparing to SCLE and ACLE. Deposition of dermal mucin highlighted by Alcian blue was found frequently in DLE and SCLE.

SUMMARY

- This prospective study was conducted in Department of Pathology, Coimbatore Medical College, Coimbatore.
- 40 skin biopsy samples received in the period of January 2017 to June 2018, were included in the study.
- In 40 clinically diagnosed CLE patients, 19 were diagnosed as ACLE, 6 as SCLE and 15 as DLE.
- The frequent / peak age of occurrence was between 31 to 45 years of age.
- Females (67.5%) were more commonly affected than males (32.5%) with female to male ratio of 2:1.
- ACLE patients commonly presented with maculopapular lesions, while SCLE and DLE patients frequently had plaque like lesions.
- Arthralgia, oral lesions, photosensitivity and crusting of lesions were commonly observed in ACLE.
- The most common site of involvement were face and scalp (60%), followed by upper extremities (30%), back (27.5%) and generalized body involvement (25%).

- ACLE patients had lesions of less than 6 months duration, SCLE with lesions of 1 to 12 months duration and DLE with lesions of 1 to 5 years of duration.
- **ACLE :** The common histopathological features of ACLE were basal cell vacuolar degeneration, mild periadnexal and perivascular inflammation, followed by epidermal atrophy and follicular plugging. Less frequently, vasculitis and basement membrane thickening were observed.
- **SCLE :** The frequently observed histological findings were basal cell vacuolar degeneration, epidermal atrophy, periadnexal and perivascular inflammation. Dermal mucin was found in 50% of cases. Basement membrane thickening was not found in any of the 6 cases of SCLE.
- **DLE :** Severe periadnexal and perivascular inflammation, basal cell vacuolar degeneration, epidermal atrophy, hyperkeratosis and follicular plugging were seen in most of the cases. Basement membrane thickening and dermal mucin were frequently observed in DLE only with the use of special stains.

- Basal cell vacuolar degeneration, periadnexal and perivascular inflammation were the common features observed in various subtypes of Cutaneous LE.
- The combination of basal cell vacuolar degeneration and epidermal atrophy along with clinical features were highly suggestive of SCLE.
- The limitations of the study is that, Direct Immunofluorescence could not be performed in all the cases. Comparison of skin biopsy findings of treated and untreated patients could add more information to the available literature.

CONCLUSION

The clinical features and distribution of cutaneous lesions in Lupus Erythematosus simulate few other dermatological diseases. Serological tests, though available are sometimes confounding. The skin biopsies, show profound variation in the combination of the actual histopathological features required for the diagnosis which can impede the pathologist from providing a conclusive diagnosis. Factors like age of the lesion, site of biopsy and non specific or atypical clinical presentations can cause variations in the histopathological findings.

In such cases, the histopathological examination along with special stain, PAS with Alcian blue and Direct immunofluorescence helps to subclassify and diagnose, based on the thickening of basement membrane and interstitial dermal mucin deposition along with the clinical features and serological tests. Since, basement membrane thickening and dermal mucin are commonly observed in chronic patients it is advisable to carry out special stain in skin biopsy samples of patients with symptoms of more than 1 year duration. Periodic review and analysis of series of cutaneous lesions of lupus erythematosus will help us to understand the variations in the manifestations of the disease in all aspects.

BIBLIOGRAPHY

1. Albrecht J, Berlin JA, Braverman IM, et al. Dermatology position paper on the revision of the 1982 ACR criteria for systemic lupus erythematosus, Lupus 2004;13;839-849.

2. Sontheimer RD, Thomas JR, Gilliam JN. Subacute CLE. Arch Dermatol 1979; 115:1409-15.

3. Cannon EF, Curtis AC. A Survey of LE in the University of Michigan Hospital since 1948. Arch Dermatol 1958; 78: 196-9

4. Rowell NR. The natural history of lupus erythematosus. *Clin Exp Dermatol* 1984; **9**: 217–31.15

5. Millard LG, Rowell NR. Abnormal laboratory test results and their relationship to prognosis in discoid lupus erythematosus. *Arch Dermatol* 1979; **115**: 1055–8.

6. Ganor S, Sagher F. SLE changing to the chronic discoid type. Dermatologica 1962; 125:81-92.

7. Grönhagen CM, Nyberg F. Cutaneous lupus erythematosus: An update. Indian Dermatol Online J 2014;5:7-13

8. Tuffanelli DL. Cutaneous immunopathology: recent observation. J Invest Dermatol 1975; 65:143-53.

9. Malaviya AN[1], Singh RR, Singh YN, et al, Prevalence of systemic lupus erythematosus in India.1993 Apr;2(2):115-8.

10. Jordan C Achtman and Victoria P Werth Pathophysiology of cutaneous lupus erythematosus .Arthritis Res Ther. 2015; 17(1): 182.

11. Yu C, Chang C, Zhang J. Immunologic and genetic considerations of cutaneous lupus erythematosus: a comprehensive review. J Autoimmun. 2013;41:34–45. doi: 10.1016/j.jaut.2013.01.007.

12. Bijl M, Kallenberg CG. Ultraviolet light and cutaneous lupus. *Lupus* 2006;**15**: 724–7.

13. Meller S, Winterberg F, Gilliet M, Muller A, Lauceviciute I, Rieker J, et al. Ultraviolet radiation-induced injury, chemokines, and leukocyte recruitment: an amplification cycle triggering cutaneous lupus erythematosus. Arthritis Rheumatol. 2005;52: 1504–1516. doi: 10.1002/art.21034

14. Foering K, Chang AY, Piette EW, Cucchiara A, Okawa J, Werth VP. Characterization of clinical photosensitivity in cutaneous lupus erythematosus. J Am Acad Dermatol. 2013;69:205–213. doi: 10.1016/j.jaad.2013.03.015.

15. Lin JH, Dutz JP, Sontheimer RD, Werth VP. Pathophysiology of cutaneous lupus erythematosus. Clin Rev Allergy Immunol. 2007;33:85–106. doi: 10.1007/s12016-007-0031-x

16. Norris DA, Whang K, DavidBajar K, Bennion SD. The influence of ultraviolet light on immunological cytotoxicity in the skin. Photochem Photobiol. 1997;65:636–646. doi: 10.1111/j.1751-1097.1997.tb01905.x.

17. Kuhn A, Herrmann M, Kleber S, Beckmann-Welle M, Fehsel K, Martin-Villalba A, et al. Accumulation of apoptotic cells in the epidermis of patients with cutaneous lupus erythematosus after ultraviolet irradiation. Arthritis Rheumatol. 2006;54:939–950. doi: 10.1002/art.21658

18. Chen XW, Shen Y, Sun CY, Wu FX, Chen Y, Yang CD. Anti-class A scavenger receptor autoantibodies from systemic lupus erythematosus patients impair phagocytic clearance of apoptotic cells by macrophages in vitro. Arthritis Res Ther. 2011;13:R9. doi: 10.1186/ar3230.

19. Biazar C, Sigges J, Patsinakidis N, Ruland V, Amler S, Bonsmann G, et al. Cutaneous lupus erythematosus: first multicenter database analysis of 1002 patients from the European Society of Cutaneous Lupus Erythematosus(EUSCLE) Autoimmun Rev. 2013;12:444–454. doi: 10.1016/j.autrev.2012.08.019.

20. Li PH, Wong WHS, Lee TL, Lau CS, Chan TM, Leung AMH, et al. Relationship between autoantibody clustering and clinical subsets in SLE: cluster and association analyses in Hong Kong Chinese. Rheumatology. 2013;52:337–345.

21. Wasicek CA, Reichlin M. Clinical and serological differences between systemic lupus erythematosus patients with antibodies to Ro versus patients with antibodies to Ro and La. J Clin Invest. 1982;69:835–843. doi: 10.1172/JCI110523.

22. Jost SA, Tseng LC, Matthews LA, Vasquez R, Zhang S, Yancey KB, Chong BF. IgG, IgM, and IgA antinuclear antibodies in discoid and systemic lupus erythematosus patients. Sci World J. 2014;2014:171028. doi: 10.1155/2014/171028.

23. David E et al. Lever Histopathology of skin 10th edition: 425-37

24. De Berker D, Dissaneyeka M, Burge S. The sequelae of chronic cutaneous lupus erythematosus. Lupus 992;1:181.

25. Patel P, Werth V. Cutaneous lupus eryhtematosus: a review. Dermatol Clin 2002;20:373-385.

26. Estes D, Christian CL. The natural history of systemic lupus erythematosus by prospective analysis. Medicine (Baltimore) 1971;50:85.

27. Wojnarowska F. Simultaneous occurrence in identical twins of discoid lupus erythematosus and polymorphic light eruption. *J R Soc Med* 1983; **76**: 791–2.

28. Millard TP, Kondeatis E, Vaughan RW *et al.* Polymorphic light eruption and the HLA DRB1*0301 extended haplotype are independent risk factors for cutaneous lupus erythematosus. *Lupus* 2001; **10**: 473–9.

29. Millard LG, Rowell NR, Rajah SM. Histocompatibility antigens in discoid and systemic lupus erythematosus. *Br J Dermatol* 1977; **96**: 139.

30. Akasu R, Kahn HJ, From L. Lymphocyte markers on formalin – fixed tissue in Jessner's lymphocytic infiltrate and lupus erythematosus. J Cutan Pathol 1992;19:59.

31. Griffiths C, Barker J et al. Rook's textbook of Dermatology 8th edition; Vol 3: 2480-82.

32. Rothfield N, March CH, Miescher P *et al.* Chronic discoid lupus erythematosus. *N Engl J Med* 1963; **269**: 1155–61.

33. Wilson CL, Burge SM, Dean D *et al.* Scarring alopecia in discoid lupus erythematosus. *Br J Dermatol* 1992; **126**: 307–14.

34. Paramsothy Y, Lawrence CM. 'Tin-tack' sign in localized pemphigus foliaceus. *Br J Dermatol* 1987; **116**: 127–9.

35. David W; skin pathology Churchill Livingston Elsevier Publication 3rd edition 2010:41, 57-63,73.

36. Shuster S. A simple sign of discoid lupus erythematosus. *Br J Dermatol* 1981; **104**: 350–1.

37. George PM, Tunnessen WW. Childhood discoid lupus erythematosus. *Arch Dermatol* 1993; **129**: 613–7.

38. Millard LG, Rowell NR. Chilblain lupus erythematosus (Hutchinson). *Br J Dermatol* 1978; **98**: 497–506.

39. Aoki T, Ishizawa T, Hozumi Y *et al.* Chilblain lupus erythematosus of Hutchinson responding to surgical treatment: a report of two patients with anti-Ro/SS-A antibodies. *Br J Dermatol* 1996; **134**: 533–7.

40. Kint A, van Herpe L. Ungual anomalies in lupus erythematosus discoides. *Dermatologica* 1976; **153**: 298–302.

41. Burge SM, Frith PA, Juniper RP *et al.* Mucosal involvement in systemic and chronic cutaneous lupus erythematosus. *Br J Dermatol* 1989; **121**: 727–41.

42. Tosti A, Tosti G, Giovannini A. Discoid lupus erythematosus solely involving the eyelids: report of three cases. *J Am Acad Dermatol* 1987; **16**: 1259–60.

43. Vinciullo C. Hypertrophic lupus erythematosus: differentiation from squamous cell carcinoma. Australas J Dermatol 1986;27:76.

44. Ueki H, Wolff HH, Braun- Falco O. Cutaneous localization of human gamma globulins in lupus erythematosus. Arch Dermatol Forsch 1974; 248:297.

45. Ruiz H, Sanchez JL. Tumid lupus erythematosus. Am J Dermatopathol 1999; 12:356.

46. Spann CR, Callen JP, Klein JB *et al.* Clinical, serologic and immunogenetic studies in patients with chronic cutaneous (discoid) lupus erythematosus who have verrucous and/or hypertrophic skin lesions. *J Rheumatol* 1988; **15**: 256–61.

47. Ng PP, Tan SH, Tan T. Lupus erythematosus panniculitis: a clinicopathologic study. *Int J Dermatol* 2002; **41**: 488–90.

48. de Berker D, Burge S, Dissaneyeka M. The sequelae of chronic cutaneous lupus erythematosus. *Lupus* 1992; **1**: 181–6.

49. Tebbe B, Mansmann U, Wollina U *et al.* Markers in cutaneous lupus erythematosus indicating systemic involvement: a multicentre study of 296 patients. *Acta Derm Venereol (Stockh)* 1997; **77**: 305–8.

50. Griffiths C, Barker J et al. Rook's textbook of Dermatology 8th edition; Vol 3: 2496-97, 2506.

51. Mellers S, Winterberg F, Gilliet M *et al.* Ultraviolet radiation-induced injury, chemokines and leukocyte recruitment. *Arthritis Rheum* 2005; **52**: 1504–16.

52. Popovic K, Brauner S, Ek M *et al.* Fine specifi city of the Ro/SSA autoantibody response in relation to serological and clinical findings in 96 patients with selfreported cutaneous symptoms induced by sun. *Lupus* 2007; **16**: 10–7.

53. Sontheimer RD. Subacute cutaneous lupus: a 25 year evolution of a prototypic subset (subphenotype) of lupus erythematosus defi ned by characteristic cutaneous, pathological, immunological and genetic fi ndings. *Autoimmun Rev* 2005; **4**: 253–63.

54. Hochberg MC. The incidence of systemic lupus erythematosus in Baltimore, Maryland, 1970–77. *Arthritis Rheum* 1985; **28**: 80–6.

55. Tan EM, Cohen AS, Fries JF , et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1982;25:1271.

56. Griffiths C, Barker J et al. Rook's textbook of Dermatology 8th edition; Vol 3: 2530.

57. Block SR, Lockshin MD, Winfi eld JB *et al.* Immunologic observations on nine sets of twins either concordant or discordant for SLE. *Arthritis Rheum* 1976; **19**: 545–54.

58. Reveille JD, Bias WB, Winkelstein JA *et al.* Familial systemic lupus erythematosus: immunogenetic studies in eight families. *Medicine* 1983; **62**: 21–35.

59. Alarcón-Segoviá D. The pathogenesis of immune dysregulation in systemic lupus erythematosus. A Troika. *J Rheumatol* 1984; **11**: 588–90.

60. Ramirez F, Williams RC, Sibbitt WL *et al.* Immunoglobulin from systemic lupus erythematosus serum induces interferon release by normal mononuclear cells. *Arthritis Rheum* 1986; **29**: 326–36.

61. Hughes P, Holt S, Rowell NR *et al.* Thymus-dependent (T) lymphocyte deficiency in progressive systemic sclerosis. *Br J Dermatol* 1976; **95**: 469–73.

62. Werth VP. Cutaneous lupus: insights into pathogenesis and disease classifi cation. *Bull NYU Hosp Jt Dis* 2007; **65**: 200–4.

63. Mok CC, Lau CS Pathogenesis of systemic lupus erythematosus *Journal of Clinical Pathology* 2003;**56:**481-490.

64. Yell JA, Allen J, Wojnarowska F, Kirtschig G, Burge SM. Bullous systemic lupus erythematosus: revised criteria for diagnosis. *Br J Dermatol* 1995; **132**: 921–8.

65. Meurer M .Immunopathology of cutaneous lupus erythematosus; chapter 22: 306

66. Rowell NR, Scott DG. Immunohistological studies with anti-connective tissue and anti-immunoglobulin antisera of the skin in lupus erythematosus and scleroderma. *Br J Dermatol* 1975; **93**: 431–41.

67. Leibowitch M, Droz D, Noel LH *et al.* C1q deposits at the dermoepidermal junction: a marker discriminating for discoid and systemic lupus erythematosus. *J Clin Immunol* 1981; **2**: 119–24.

68. Bharti S, Dogra S, Saikia B, Walker RM, Chhabra S, Saikia UN. Immunofluorescence profile of discoid lupus erythematosus. Indian J Pathol Microbiol 2015;58:479-82

69. Dahl MV. Usefulness of direct immunofl uorescence in patients with lupus erythematosus. *Arch Dermatol* 1983; **119**: 1010–7

70. Mysorekar VV, Sumathy T K, Shyam Prasad A L. Role of direct immunofluorescence in dermatological disorders. Indian Dermatol Online J 2015;6:172-80

71. Chhabra S, Minz RW, Saikia B. Immunofluorescence in dermatology. Indian J Dermatol Venereol Leprol 2012;78:677-91

72. Kuhn A, Sonntag M, Lehmann P *et al.* Characterization of the infl amatory infiltrate and expression of endothelial cell adhesion molecules in lupus erythematosus tumidus. *Arch Dermatol Res* 2002; **294**: 6–13.

73. McCreight WG, Montgomery H; Cutaneous changes in lupus erythematosus. Archives of Dermatology and syphilology, 1950; 61(1):1-11.

74. Bangert JL, Freeman RG, Sontheimer RD, Gilliam JN; Subacute cutaneous lupus erythematosus and discoid lupus erythematosus. Arch Dernatol.,1984; 120(3):332-337.

75. Kathleen M, David B, Bennion SD, DeSoain JD et al. Clinical, histologic and immunofluorescent distinctions between subacute cutaneous lupus erythematosus and discoid lupus erythematosus. J Invest Dermatol., 1992; 99:251-257.

76. Karumbaiah KP, Kariappa TM; A Histopathological Study of Cutaneous Lupus Erythematosus. Sch. J. App. Med. Sci., 1(6):765-768.

77. Bancroft, John D, Christopher Layton, and S K. Suvarna. *Bancroft's Theory and Practice of Histological Techniques.* , 2013; 230-31.

78. Aviles Izquierdo N, Cano Martinez, P. Lazaro Ochaita. Epidemiological characteristics of patients with Cutaneous Lupus Erythematosus; Actas Dermo-Sifiliograficas (English edition), Volume 105, Issue 1, January- February 2014, pages 69-73.

79. Baizar C, Sigges J, Patsinakidis N, Ruland V, Amler S, et al. (2013) Cutaneous Lupus Erythematosus : first multicenter database analysis of 1002 patients from the European Society of Cutaneous Lupus Erythematosus (EUSCLE), Autoimmun Rev 12: 444-454.

80. Gronhagen CM, Fored CM, Granath F, Nyberg F (2011) Cutaneous Lupus Erythematosus and the association with systemic lupus erythematosus: a population based cohort of 1088 patients in Sweden. Br J Dermatol 164: 1335- 1341.

81. Vera Recabarren MA, Garcia Carrasco M, Cervera R, Herrero C (2016) Comparative analysis of Acute Cutaneous Lupus Erythematosus with Subacute and Chronic Cutaneous Lupus Erythematosus: Clinical and Immunological Study of 308 patients. J Arthritis 5:185. Doi:10.4172/2167-7921.1000185.

PROFORMA

COIMBATORE MEDICAL COLLEGE

Department of Pathology

Coimbatore

PARTICULARS OF THE PATIENT:

Name	:	Ward	:
Age (years)	:	IP No	:
Sex	:	Occupation	:

CHIEF COMPLAINTS :

HISTORY OF PRESENTING ILLNESS :

Skin lesions

Itching

Fever

Oral lesions

Arthralgia

Photosensitivity

PAST HISTORY:

Drug Intake

Proceeding viral infection

FAMILY HISTORY

CLINICAL EXAMINATION AND DIAGNOSIS:

HISTOPATHOLOGICAL EXAMINATION OF SKIN BIOPSY:

SPECIAL STAINS :

Periodic Acid Schiff

Alcian Blue

FINAL DIAGNOSIS:

ஒப்புதல் படிவம்

பெயர் :

வயது:

பாலினம்:

முகவரி:

கோவை அரசு மருத்துவக் கல்லூரி மருத்துவமனையில் மருத்துவர் தலைமையில் நடைபெறும் இந்த ஆய்வில் முழு சம்மதத்துடன் கலந்து கொள்ள சம்மதிக்கிறேன். இந்த ஆய்வில் என்னை பற்றி விவரங்களை பாதுகாப்புடன் இந்த ஆய்வில் வெளியிட ஆட்சேபணை இல்லை என்று தெரிவித்துக் கொள்கிறேன். எந்த நேரத்திலும் ஆய்வில் இருந்து விலக்கிக் கொள்ளும் உரிமை உண்டு என்று அறிவேன்.

இடம்:

தேதி:

கைகெயாப்பம்/
ரேகை

MASTER CHART

S NO	IP NO.	AGE	SEX	SITE	DURATION	TYPE OF LESION									HISTOPATHOLOGICAL CHANGES										clinical diagnosis	pathological diagnosis	PAS with alclan blue
						papules	macules	Plaques	itching	crusting	fever	arthralgia	oral lesions	photosensitivity	Hyperkeratosis	perifollicular fibrosis	epidermal atrophy	BM Thickening	periadnexal and perivascular inflammation	Follicular plugging	basal cell vacuolation	Subepidermal edema and dermal mucin	melanin incontinence	vasculitis			
1	601	30	F	Bilateral trunk, malar area ,NL fold	10 days	+	+	+	+	-	+	+	+	-	-	-	-	-	+	+	+	-	+	-	ACLE	ACLE	-
2	196	28	F	Scalp,face, back ,bilateral upper limbs	2 weeks	+	-	+	-	+	+	+	+	+	-	-	+	-	+	-	+	-	+	-	ACLE	ACLE	-
3	859	38	M	Face, chest,upper back	1 year	-	-	+	-	-	-	-	-	-	+	-	-	-	+	-	+	+	-	-	DLE	DLE	Mucin+
4	692	41	F	Face, chest, foot, bacl and upper limbs	6 months	-	-	+	-	+	-	+	-	+	+	-	+	-	+	+	-	-	+	-	DLE	DLE	-
5	2083	29	F	back, legs and dorsum of foot	10 days	+	-	+	-	-	+	-	-	+	-	+	+	-	+	-	-	-	-	-	ACLE	ACLE	-
6	2314	25	F	all over the body	6 months	+	-	-	+	-	+	+	-	-	-	-	-	-	+	-	-	-	-	+	ACLE	ACLE	-
7	2016	53	M	shoulder and arm	3 months	+	-	+	-	+	-	-	-	-	-	-	+	-	+	-	+	+	-	-	EMF	SCLE	Mucin+
8	4377	75	M	scalp, knees, legs, thigh and back	3 months	-	-	+	-	+	-	-	-	-	+	-	-	+	+	-	-	-	-	-	ACLE	ACLE	BMT+
9	2657	35	M	face. Arms and back	1 year	-	-	+	+	-	-	+	+	-	-	-	+	+	+	-	+	+	+	-	DLE	DLE	Mucin+; BMT+
10	2795	38	F	all over the body	10 days	+	+	-	-	-	-	+	+	-	-	-	+	-	+	+	-	-	-	-	ACLE	ACLE	-
11	3470	36	F	all over the body	5 years	+	+	-	-	+	-	+	+	+	-	-	+	-	+	+	-	-	-	+	ACLE	ACLE	-
12	3942	60	F	scalp, forearm	1 week	+	-	-	-	+	+	+	-	-	-	-	+	-	+	+	+	-	+	-	ACLE	ACLE	-
13	3812	32	F	left elbow and knee	10 years	+	-	-	-	-	-	-	-	-	-	-	+	-	+	+	-	-	-	-	HANSEN	DLE	-
14	1837	31	F	face, neck and scalp	1 year	-	-	+	-	-	-	-	-	+	+	-	-	-	+	+	+	+	+	-	DLE	DLE	Mucin+
15	1112	57	M	all over the body	4 months	+	-	-	+	-	-	-	-	-	-	-	+	-	+	+	-	-	-	-	SCLE	SCLE	-
16	3042	30	F	cheek, malar area and elbow	2 weeks	+	-	+	-	+	+	-	-	-	+	-	-	-	+	-	+	+	-	-	ACLE	ACLE	Mucin+
17	2772	40	M	face, chest,abdomen and back	1 month	+	-	+	-	-	-	-	-	-	-	-	+	-	+	+	+	-	-	-	ACLE	ACLE	-
18	3336	36	F	face., malar area and back	3 months	-	-	+	-	+	-	+	+	+	+	-	-	-	-	+	+	-	-	-	ACLE	ACLE	-
19	3508	37	F	face, back,chest and upper limbs	6 months	-	-	+	-	+	+	+	+	-	-	-	+	-	+	-	+	-	+	-	ACLE	ACLE	BMT+
20	2532	73	F	all over the body	2 years	-	-	+	+	-	-	-	+	-	+	-	-	-	+	-	+	-	+	-	ACLE	DLE	-

S NO	IP NO.	AGE	SEX	SITE	DURATION	TYPE OF LESION									HISTOPATHOLOGICAL CHANGES										clinical diagnosis	pathological diagnosis	PAS with alclan blue
						papules	macules	Plaques	itching	crusting	fever	arthralgia	oral lesions	photosensitivity	Hyperkeratosis	perifollicular fibrosis	epidermal atrophy	BM Thickening	periadnexal and perivascular inflammation	Follicular plugging	basal cell vacuolation	Subepidermal edema and dermal mucin	melanin incontinence	vasculitis			
21	4239	42	M	back, chest and face	2 months	+	-	-	-	-	-	-	-	-	+	-	-	+	+	-	+	+	-	-	ACLE	ACLE	Mucin+; BMT+
22	2372	46	M	all over the body	2 months	+	-	+	+	-	-	-	-	-	-	-	+	-	+	-	+	-	+	-	ACLE	ACLE	-
23	3100	48	F	scalp, face, neck and chest	4 months	-	-	-	-	+	-	+	-	+	-	-	+	-	+	-	-	-	-	-	ACLE	ACLE	-
24	2563	40	F	all over the body	15 years	+	-	-	-	+	-	-	-	-	+	-	-	+	+	-	+	-	-	-	ACLE	DLE	BMT +
25	1649	28	M	all over the body	2 years	-	-	+	-	+	-	-	-	-	+	-	-	+	+	+	-	+	-	+	DLE	DLE	Mucin +; BMT +
26	1603	55	M	face, trunk,upper and lower limbs	6 months	-	-	+	-	+	-	-	-	-	+	-	-	-	+	-	-	+	-	-	SCLE	SCLE	-
27	1306	54	F	face, chest and back	2 years	-	-	+	-	-	-	-	-	-	-	-	+	-	+	-	+	+	-	-	ACLE	DLE	Mucin+
28	1942	56	F	face and abdomen	1 year	-	-	+	-	-	-	-	-	-	-	-	+	-	+	+	+	+	-	-	DLE	DLE	Mucin+
29	73	17	F	face, scalp and trunk	3 months	+	-	+	-	+	-	+	-	-	-	-	+	+	-	+	+	-	-	-	ACLE	ACLE	BMT+
30	434	36	F	knee and forearm	3 months	+	-	+	+	-	+	+	-	-	+	-	-	-	+	+	+	-	-	-	ACLE	ACLE	-
31	380	47	F	face, trunk and chest	2 months	+	-	-	-	+	+	-	+	-	-	-	+	+	-	+	-	-	-	-	ACLE	ACLE	BMT+
32	384	41	M	palms and trunk	7 years	-	-	+	+	-	+	+	+	+	+	-	-	-	+	+	+	+	-	-	DLE	DLE	Mucin+
33	671	17	F	upper and lower limbs	2 months	-	-	-	-	-	+	+	+	+	-	-	+	-	+	-	+	+	+	-	DLE	DLE	Mucin+
34	672	65	F	scalp	1 year	-	-	+	-	+	-	-	+	-	-	-	+	-	+	-	+	-	-	-	DLE	DLE	-
35	771	34	F	scalp and nipple	6 months	-	-	+	-	+	-	-	-	-	+	+	-	-	+	+	+	-	-	-	ACLE	SCLE	-
36	1052	65	M	all over the body	1 year	-	-	+	-	+	-	-	-	+	-	-	+	-	+	-	+	+	-	-	SCLE	SCLE	Mucin+
37	1011	27	M	bilateral arms, chest and malar area	1.5 years	-	-	-	+	-	-	-	-	-	+	-	+	+	+	-	+	+	+	-	DLE	DLE	Mucin+;BMT+
38	868	27	F	all over the body	15 days	+	+	+	-	+	+	+	-	+	+	-	+	-	+	-	+	-	+	-	SCLE	SCLE	Mucin+
39	2319	35	F	scalp and oral cavity	6 months	-	-	-	+	-	-	-	+	-	+	+	+	+	+	-	+	+	-	-	DLE	DLE	Mucin +; BMT +
40	1868	39	F	face	1 month	+	+	-	-	+	-	-	-	-	+	-	-	-	+	-	+	-	+	-	ACLE	ACLE	-

KEYWORDS: BMT – BASEMENT MEMBRANE THICKENING ; PAS – PERIODIC ACID SCHIFF